the Journal
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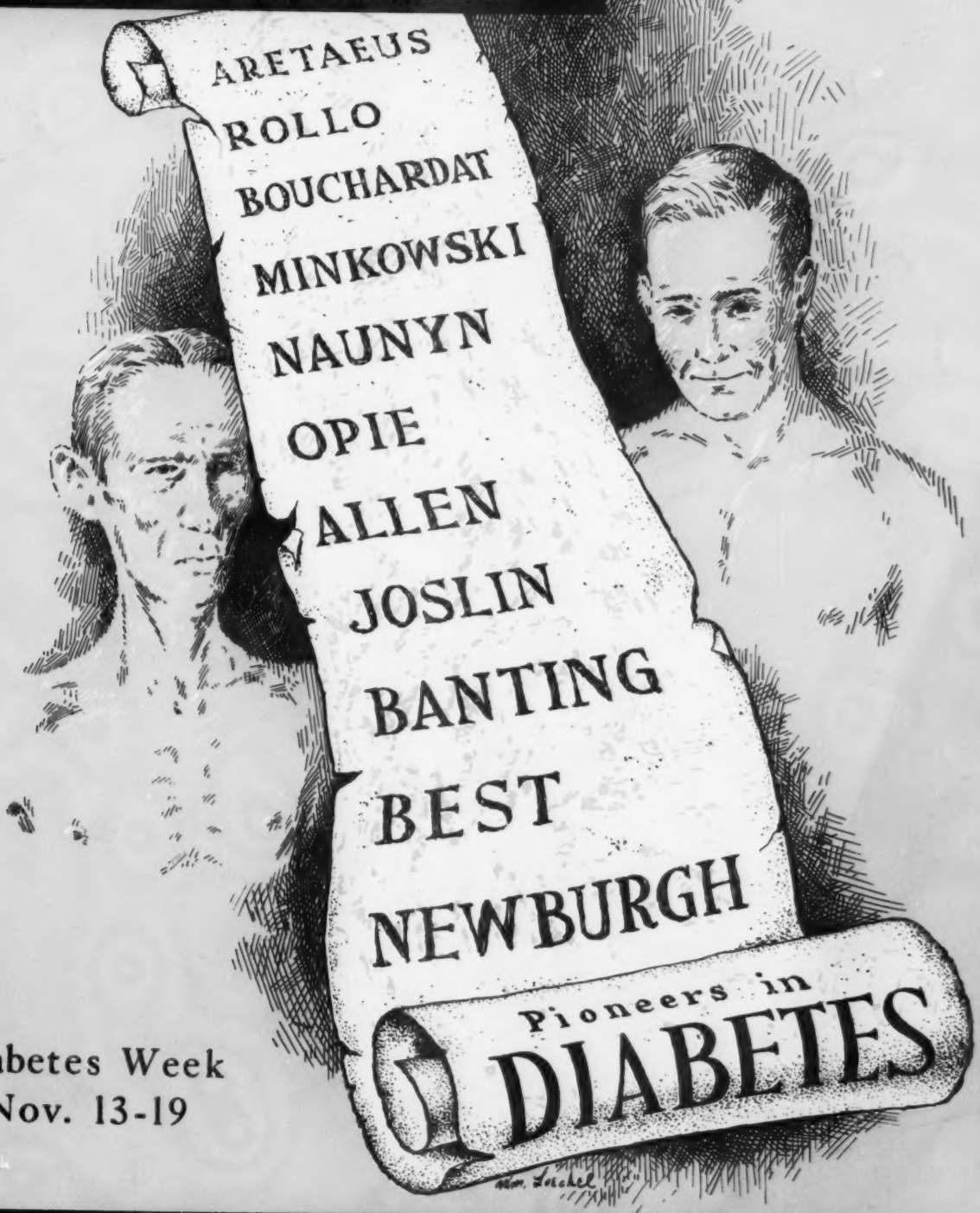

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(1) Abraham, W., in Green, J. R., & Steelman, H. F.: Epileptic Seizures, Baltimore, Williams & Wilkins Company, 1956, p. 132. (2) Crawley, J. W.: M. Clin. North America 42:317 *(March) 1958. (3) Bray, P. F.:* Pediatrics 23:151, *1959.*

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THE COVER

This number of the Journal is dedicated to Diabetes and the cover art salutes eleven "Pioneers in Diabetes" for their contributions in the medical attack against this disease.

IN THIS ISSUE

STATE SOCIETY SECTION 1473
"Campaign for Freedom" 1473
Highlights of MSMS Council Meeting—August 24, 1960 1474

PUBLIC RELATIONS 1483
"As Others See Us" 1483
MSMS Distributes Message in State Fair Exhibit 1486

SOCIO ECONOMICS 1491
State MD's Contribute to Medical Colleges 1491
Benefits Set Faster Pace 1491
More than Half of Federal Workers Enroll in Blue Cross- Blue Shield.. 1491

CLINICAL 1513
Insulin, Diabetes and Adipose Tissue—*George F. Cahill, Jr., M.D.* 1513
An Integrated View of Glucagon—*S. O. Waife, M.D.* 1519
Insulin Resistance—*James B. Field, M.D.* 1524
Differential Diagnosis of Hyperglycemia and Melituria—*William Locke, M.D.* 1528
Ocular Manifestations of Diabetes—*Lorand V. Johnson, M.D.* 1533
What Can Be Expected of the Glucose Tolerance Test?—*Raymond E. Fuller, M.D.* 1535
The Intravenous Tolbutamide Response Test—Initial Observations—*Fred W. Whitehouse, M.D.*, and *William L. Lowrie, M.D.* 1540
The Federal Government and the Nation's Health—*Aims C. McGuinness, M.D.* 1543
Immunization of Infants with Quadruple Antigens—*S. J. Giammona, M.D., C. Cookingham, M.D.*, and *E. H. Watson, M.D.* 1547
Effectiveness of Resins in the Treatment of Hyperkalemia—*John M. Weller, M. D., James M. Pierce, Jr., M.D.*, and *Donovan H. Givens, Jr., M.D.* 1551
Medical and Neurological Management of the Patient with Cerebral Vascular Accident—*Matthew S. Atkinson, M.D.* 1555

EDITORIAL 1559
National Politics and Medical Interests 1559
Congressional Action 1559
Carry On 1560
Campaign for Freedom 1560
Hypophysectomy and Retinopathy 1560
Physicians as Detectives of Diabetes 1561
Oral Hypoglycemic Agents 1561
"Security" 1562

NATIONAL AND WORLD 1565
New Medical School Opens; Seven Others Planned 1565

ANCILLARY 1569
Many Doctors Placed by Health Council 1569

NEWS BRIEFS 1585
Brief and to the Point 1585

MISCELLANEOUS
Detroit Surgical Association 1563
Michigan Department of Health 1576
Pathology Comment 1578
The Michigan Diabetes Association 1580
Obstetrical Brevits 1584
In Memoriam 1592
Michigan Authors 1594
Communications 1595
Editorial Comment 1596
The Doctor's Library 1598

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Bibliography *(13 clinical studies, 858 patients)*: **1.** Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. **4.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **5.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **6.** Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. **7.** Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. **8.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression – New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **9.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **10.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **11.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **12.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. **13.** Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

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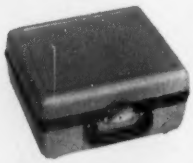
Brief-case size 

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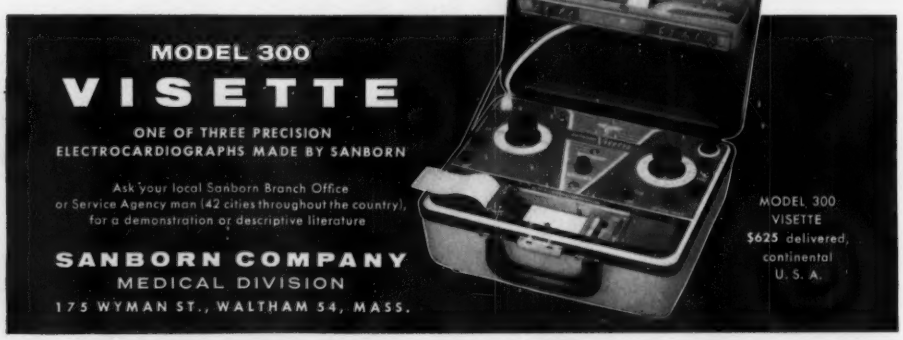

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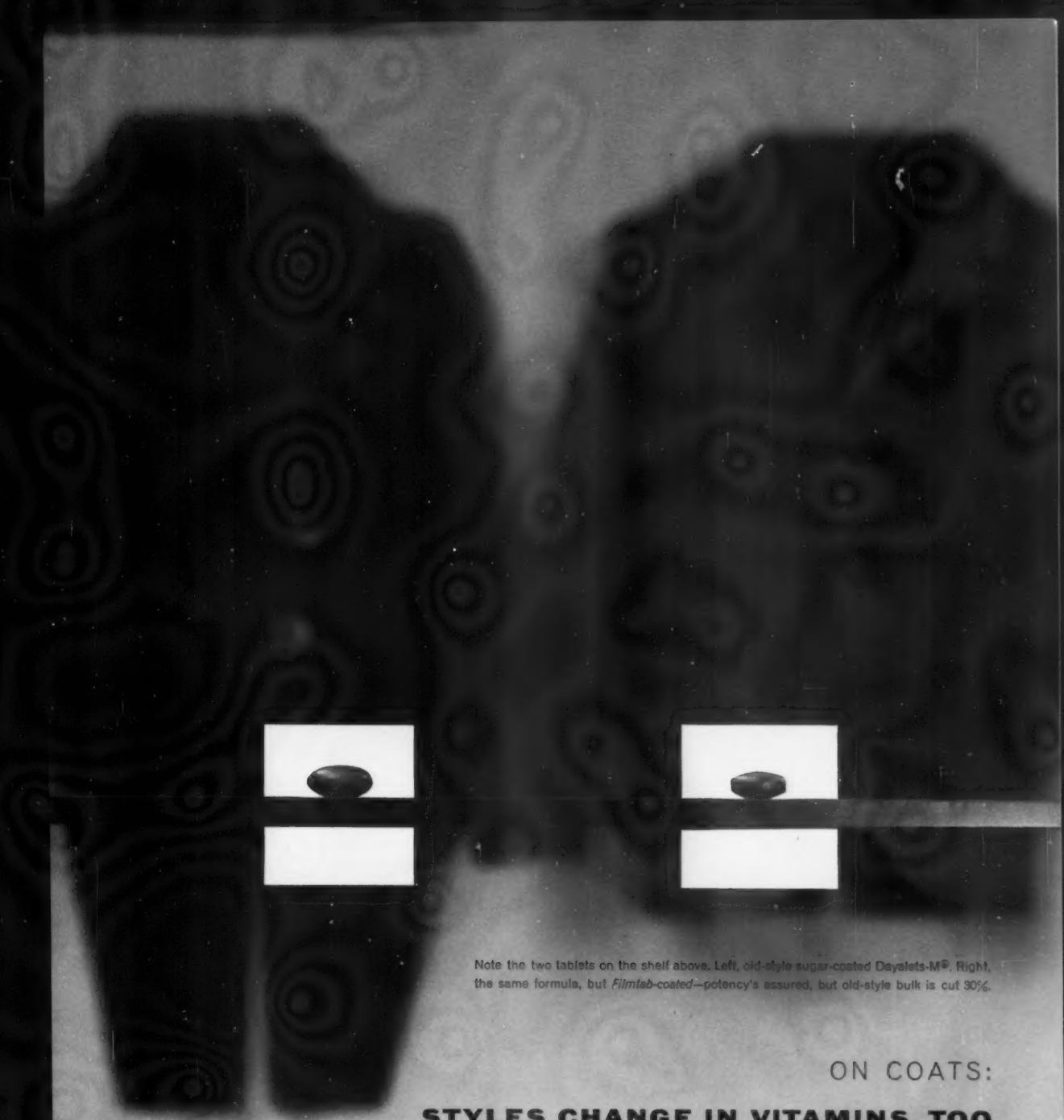

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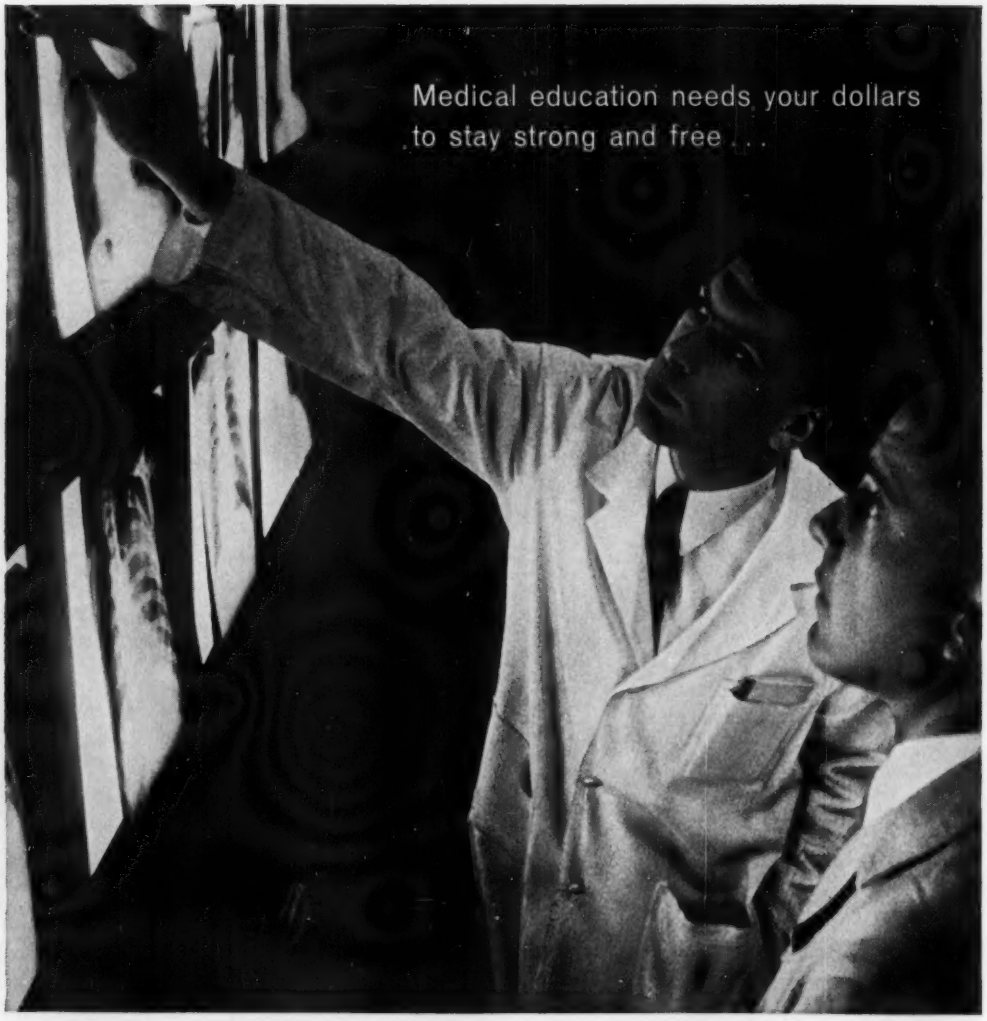

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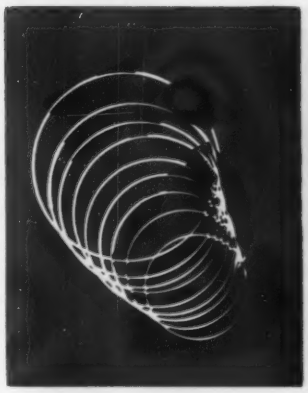

Members of the Michigan State Medical Society are now in the important Phase II of the MSMS Campaign for Freedom. And even though Phase I was a success, we can win the ultimate victory only by militant, intelligent and loyal service now.

Congratulations must be extended to many individual Michigan doctors of medicine for helping to put across Phase I of the Campaign. The Mills Bill, supported by your efforts, was approved by Congress and was signed by the President. The key vote came in the upper chamber when Senator Kennedy and other ultra-liberals backed a Forand-type amendment to the bill. In repudiation of a key plank of the Democratic platform (government health services for all the aged financed by an additional Social Security tax), and in an equally emphatic rebuke to the Democratic candidate for president, 19 of Senator Kennedy's colleagues joined with 32 Republicans to bury (51-44) the Forand issue once and for all in this session.

* * *

BITTER IN DEFEAT, Senator Kennedy vowed to "take the medical care issue to the people this fall," although Capitol insiders wonder which "people," since it was his own party's southern Democrats who voted against his proposal—and the doctors wonder what "medical care issue," in view of the fact that the legislation as passed solves the financial problems of medical care for the aged who cannot pay their own way.

The final version of the Mills Bill:

1. broadens the present state-administered welfare assistance programs with increased medical care funds for those persons dependent on social aid;
2. sets up a new federal/state grant-in-aid program to provide assistance to those people in the over-65 group who do not qualify for Old Age Assistance but are unable to pay for expensive health care costs out of their own resources;
3. lessens the penalties on social security recipients who earn more than $1200 annually, minimizing the loss of OASDI benefits for those able and willing to work after their formal retirement.

A provision which would have blanketed physicians into compulsory coverage of the social security act was deleted by the Senate before final passage.

* * *

DURING PHASE I of the Campaign for Freedom, it became increasingly clear that Medicine's job actually has only begun. There can be no question that the ultra-liberals will continue to press for adoption of socialistic legislation in the next and succeeding Congresses. Only one battle has been won. Between now and the

(Continued on Page 1479)

HIGHLIGHTS of MSMS Council Meeting

Meeting of August 24, 1960

Some sixty-six items were presented to and discussed in details by The Council at its August meeting in Lansing at which 20 members of The Council were present. The meeting was also attended by Don M. McLean, M.D., President-Elect of the Wayne County Medical Society and W. N. Hubbard, Jr., M.D., Dean of the University of Michigan Medical School.

- B. T. Montgomery, M.D., of Sault Ste. Marie, resigned as Councilor of the Twelfth District, effective September 25. The Council placed a vote of thanks on its minutes to Doctor Montgomery for his long and splendid service as a Council member.
- Request of Michigan Department of Health for MSMS co-sponsorship of Michigan Conference on Comparative Medicine, October, 1961: an observer to the Planning Committee meeting of September 15 was authorized; decision regarding sponsorship is to be on The Council's September 25 agenda.
- Councilor Conferences. Chairman Meier stated he had received reports of seven Councilor Conferences held up to August 23. The balance of the Conferences are scheduled for late August and early September.
- AMA letter containing resolutions of its 1960 (June) House of Delegates meeting urging certain actions by constituent state and component county medical societies, was reviewed and ordered referred to all Michigan county medical societies. Subject matter of the three resolutions were: (a) National Foundation; (b) role of physicians in public affairs; (c) prospective medical students.
- Michigan Hospital Association request for exchange of representation between its and the MSMS Legislative Committees was approved: The Chairman of the MSMS Legal Affairs Committee was authorized to accept invitation to serve on the MHA Legislative Committee and the Chairman of the MHA Legislative Committee (John J. Powers) was invited to serve in a similar capacity on the MSMS Legal Affairs Committee.
- AMA Woman's Auxiliary President Mrs. Wm. G. Mackersie, of Detroit. The Council recognized the high position accorded this Michigan lady and instructed that suitable recognition be rendered to her during the 1960 MSMS Annual Session in Detroit.
- Wilfrid Haughey, M.D., long-time Editor of JMSMS and former Secretary of the Society, was recognized by The Council on attaining his 80th birthday (August 10, 1960).
- New Field Secretary. After reviewing the advice of the Wayne County Medical Society representatives who attended this meeting, the special hiring committee selected E. Ray Scott for the position.
- More detailed information regarding Council deliberations. President-Elect K. H. Johnson, M.D., read a statement appearing in August 18, Detroit Medical News, which suggested more detailed information re Council actions. Doctor Johnson reported that The Council minutes now have reached over twenty pages per month and that the verbatim reports of The Council discussion did not seem feasible. Detailed as they are, the minutes would require amplification by a member of The Council if a particular question arose among county medical society officers or delegates. All Councilors are more than willing to answer any questions and provide any desired information upon request. The following motion was adopted unanimously by The Council:

  "The Council, authorized by delegated instruction from the House of Delegates to communicate its deliberations fully to the membership of MSMS, has forwarded to the component county societies the identical official minutes received by the individual Council members. If, however, the membership desires further detailed information, The Council cordially invites a representative of any component society to be a guest observer at any Council meeting."

  Monthly progress report on new MSMS headquarters building was presented by President-Elect K. H. Johnson, M.D., multiple listing of the present MSMS headquarters at 606 Townsend St., Lansing, was authorized for a period of 60 days (this allowed 40 members of the Lansing Realty Board the opportunity to sell this property).

  Doctor Johnson reported that, upon Council authorization, he had from time to time signed certain change orders in the headquarters building and was happy to report that the total changes to date, exclusive of a few specifically requested by MSMS, amounted to only 1½ per cent of the adjusted construction cost of the new building. The Council agreed that this was an extremely low figure.
- Campaign for Freedom. Progress report on this project was presented, including action taken by the Congress on the Mills Bill (care to the aged).

(Continued on Page 1476)

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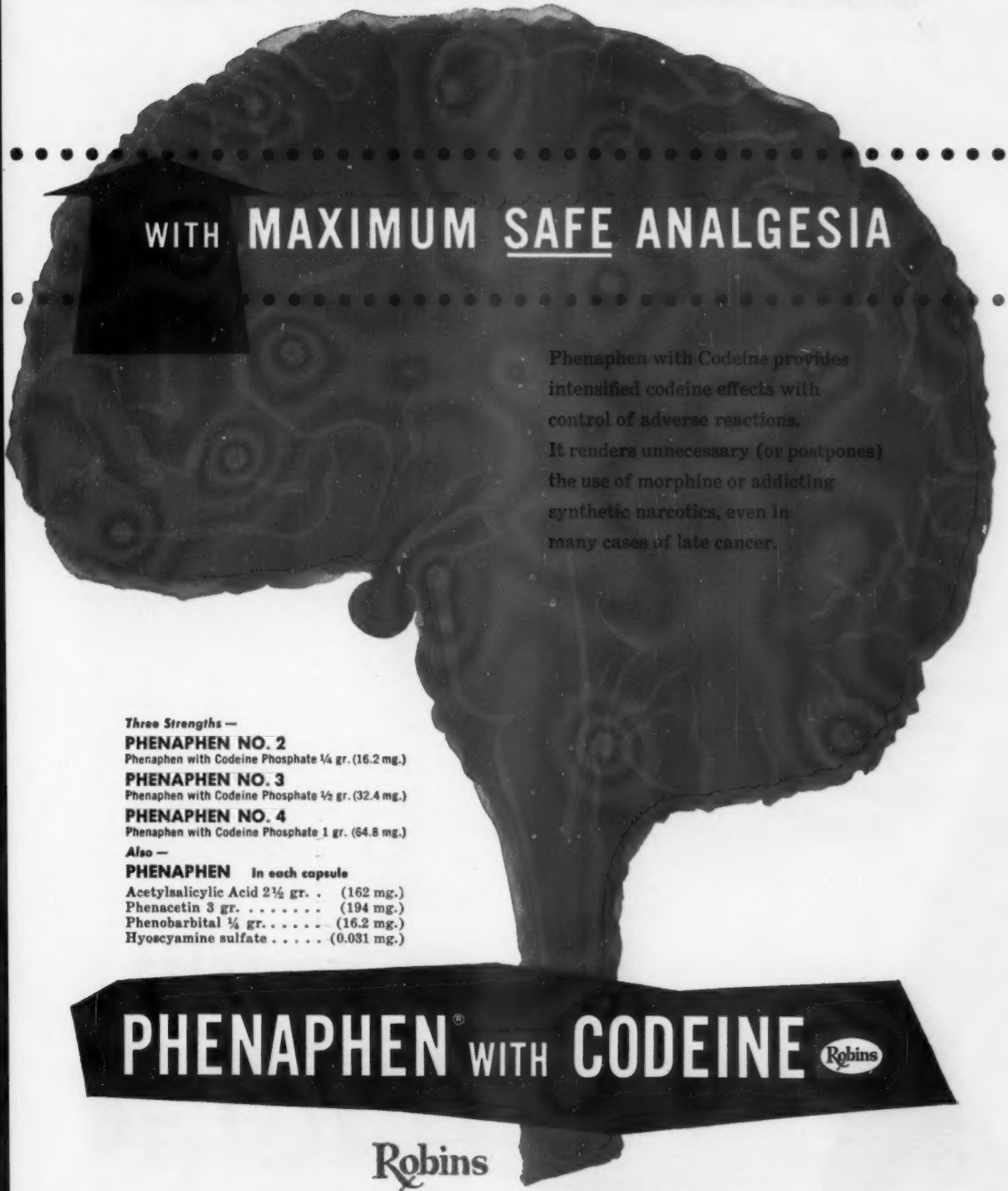

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Highlights of MSMS Council Meeting

(Continued from Page 1474)

The second phase of the Campaign—to take the MSMS message to the public and to encourage doctors to continue their interest in this election year—required additional financing so The Council authorized the expenditure of an additional $5,000.00, between now and the September 25 meeting of Council, to finance the Campaign for Freedom. Discussion brought out that specific recommendations for improving the present welfare system in Michigan in caring for the aged be developed on the State level similar to action being taken by the Washtenaw County Medical Society and that this would be desirable as a presentation to the House of Delegates. The Council stressed that the individual Councilors should go to county society meetings and urge members to become more active in their community's political and economic affairs—if MD's are not part of the community, the community will soon forget them. This is especially true in the case of newer doctors in communities. Every attempt must be made to achieve public support for Medicine's position.

- Resolution on aging. The Council unanimously adopted this following resolution:

  WHEREAS, a healthy, alert, and vital aged population constitutes one of this country's greatest human assets; and

  WHEREAS, the well being of our senior citizens depends on many factors, their environment, mental attitude, financial resources, and physical health; and

  WHEREAS, new techniques of "whole person treatment" of the senior patient in such areas as pre-retirement planning, group housing, and preventive medicine counselling, will help this group spend their golden years in comfort, health, and dignity; now therefore be it

  RESOLVED: That the members of the medical profession continue to explore new methods of treating the elderly patient; and be it further

  RESOLVED: That the medical profession proposes and supports the following 10-point program as a positive approach for preserving the health care, financial resources, and human dignity of the senior citizen:

  1. Removal of compulsory retirement provisions by industry and labor.
  2. A program to provide work opportunities for the aged.
  3. Encouragement of state and community governments to share voluntary health insurance premiums for those over 65 who need financial assistance.
  4. Participation by the medical profession in the 1961 White House Conference on Aging.
  5. Increasing cash benefits to those receiving Old Age Assistance.
  6. Expansion of OAA to share the voluntary health insurance costs of "marginally indigent" persons (those who are independent except for unusual trouble).
  7. Establishment of a privately-financed plan comparable to the Federal Deposit Insurance Corporation, underwriting health insurance premiums of those unable to maintain them.
  8. Construction of an experimental housing project for the aged near a medical school for scientific study of housing needs relative to health.
  9. An educational program emphasizing pre-retirement planning programs beginning at age 45.
  10. Emphasis on a preventive medicine program to include periodic health appraisals; control of communicable disease; improving patient care and rehabilitation in nursing homes; and the developing of chronic disease hospital units.

- Beginning with the Annual Session of 1961, out-of-Michigan guest essayists on the program will receive small honoraria as well as expenses. This action of The Council is necessary in order that the best talent be obtained for the MSMS Annual Session programs.
- Schedule for The Council's Annual Session of January 26-27-28 and also for the County Secretaries-Public Relations Seminar, January 28-29, 1961, both meetings to be held in Lansing, was approved.
- A proposal by the Carrier to the Michigan Department of Insurance to seek a ruling so that Wayne County Medical Society members, not now covered by the Wayne County Group Life Plan, might be given the opportunity to purchase the MSMS Group Plan was deferred until the advice of the Wayne County Medical Society's Council is obtained.
- Congratulations were authorized to be sent to J. W. Towey, M.D., of Powers, who on September 9 completed 38 years as an active member of MSMS and his component Society which is honoring him on this date.
- Legal Counsel's Report included opinions on: (a) blood alcohol determinations; (b) interpretation of a particular fee in the Uniform Fee Schedule for Governmental Welfare Agencies; (c) sterilization procedures.
- Public Relations Counsel's Report included recommendations from eleven Regional Conferences on Aging and a summation of same for presentation

(Continued on Page 1478)

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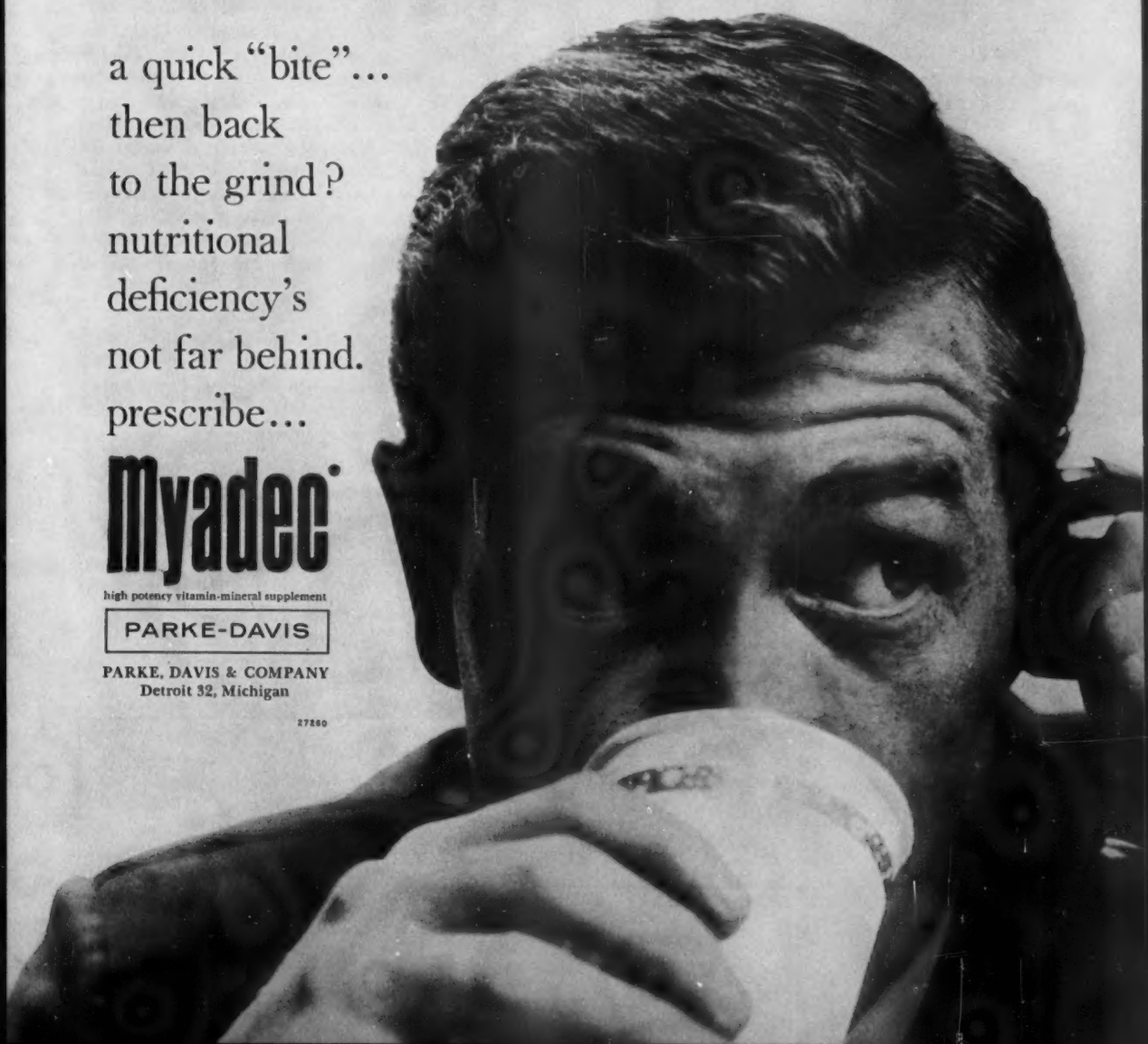

Highlights of MSMS Council Meeting

(Continued from Page 1476)

to the Michigan Commission on Aging, which The Council authorized to be sent.

- Committee reports: (a) Vocational Rehabilitation, meeting of June 30; (b) Wayne Councilor District Medical Care Insurance Committee, August 28; (c) Courses on Medical Economics and Ethics, August 10; (d) Scientific Radio, August 11; (e) progress report of ad hoc Committee on Caro Hospital Staff Situation.

- J. Joseph Herbert gavel. This significant gavel was presented from Mrs. Herbert through Councilor Wm. M. LeFevre, M.D., of Muskegon, to the Michigan State Medical Society and was accepted with thanks.

- The following MSMS representation was authorized: (a) to 1960 State Conference on Aging to be held in Lansing, September 21-22:

  F. W. Baske, M.D., 923 Maxine St., Flint
  E. F. Crippen, M.D., 126½ State St., Mancelona
  R. L. Fitts, M.D., 50 College Ave., S.E., Grand Rapids
  A. Hazen Price, M.D., 62 W. Kirby, Detroit 2
  Jack Rom, M.D., 8600 W. McNichols, Detroit 35
  C. Howard Ross, M.D., 715 University Ave., N. Ann Arbor
  F. C. Swartz, M.D., 720 Seymour St., Lansing
  V. K. Volk, M.D., Saginaw County Hospital, Box 65, Saginaw;

  (b) AMA Medical Disciplinary Committee, meeting in Chicago, September 12-13: Executive Director Wm. J. Burns was authorized to attend this meeting; (c) To American Association of Medical Assistants Convention, Dallas, in October: Glenn E. Millard, M.D., Detroit and J. W. Rice, M.D., Jackson, were requested to attend.

- Appointments: (a) Committee to Delineate and Coordinate Program to Implement Insurance Commissioner's Recommended Educational Program: H. J. Meier, M.D., Coldwater, Chairman; K. H. Johnson, M.D., Lansing; H. F. Falls, M.D., Ann Arbor; G. Thomas McKean, M.D., Detroit; Wm. M. LeFevre, M.D., Muskegon; H. H. Hiscock, M.D., Flint; D. N. Sweeny, Jr., M.D., Detroit; F. C. Swartz, M.D., Lansing; R. W. Teed, M.D., Ann Arbor; F. P. Rhoades, M.D., Detroit; J. S. DeTar, M.D., Milan; and H. W. Brenneman, as Advisor; (b) Committee to meet with Michigan State Board of Registration in Chiropody: L. A. Drolett, M.D., Chairman, Lansing; Wm. H. Blodgett, M.D., Detroit; B. M. Harris, M.D., Ypsilanti; R. J. Mason, M.D., Birmingham; G. Thomas McKean, M.D., Detroit; (c) Centennial Committee for 1965 Annual Session: K. H. Johnson, M.D., Chairman, Lansing; Milton A. Darling, M.D., Detroit; G. B. Saltonstall, M.D., Charlevoix; G. W. Slagle, M.D., Battle Creek; L. W. Hull, M.D., Detroit; R. J. Hubbell, M.D., Suttons Bay; W. S. Jones, M.D., Menominee; C. E. Umphrey, M.D., Detroit, and the future Past President until 1965; (d) 1961 Michigan Clinical Institute Program Committee: John W. Sigler, M.D., Chairman; Henry Vandenberg, Jr., M.D.; Joseph L. Posch, M.D.; Benjamin I. Johnstone, M.D.; Aaron Z. Rodgers, M.D.; George S. Fisher, M.D.; Charles G. Jennings, M.D.; and Harold C. Mack, M.D., all of Detroit; (e) Mr. Donald Walchenbach (representing Michigan Hospital Association) to Committee on National Defense; Roger B. Nelson, M.D., Ann Arbor; Earl F. Wolfman, M.D., Ann Arbor; Nicholas Gimbel, M.D., Detroit, to Committee on National Defense as Advisors.

- Future Meetings. The Council decided the dates and place of its Mid-summer session of 1963; also to hold its Annual Session of 1967 in Grand Rapids the week of September 24-29. Future Annual Sessions, therefore, are as follows:

  1961—Grand Rapids, September 24-29
  1962—Detroit, September 23-28
  1963—Grand Rapids, September 22-27
  1964—Detroit, September 27-October 1
  1965—(Centennial Convention) Detroit, September 19-24
  1966—Grand Rapids, September 25-30
  1967—Grand Rapids, September 24-29
  1968—Detroit (dates not set)
  1969—Grand Rapids (dates not set)

MICHIGAN MEDICAL MEETINGS AND CLINIC DAYS

December 1-3	Western Surgical Association	Detroit
January 28-29	MSMS County Secretaries—Public Relations Seminar	East Lansing
March 8-10	Michigan Clinical Institute	Detroit

The Journal Microfilmed

THE JOURNAL of the Michigan State Medical Society for 1959 is now microfilmed on 36 mm. tape and is obtainable for anyone who wishes to purchase it. The cost is $6.70. Address Michigan State Medical Society, 606 Townsend Street, Lansing 15, Michigan, or University Microfilms, Ann Arbor, Michigan.

THE PROVIDENCE HOSPITAL ANNUAL CLINIC DAY will be held on Wednesday, October 26, 1960, at 2500 West Grand Boulevard, Detroit. Registration will begin at 8:50. Participants in this annual clinic day will be: Francis W. Dwyer, M.D., Chief of Staff, Providence Hospital; A. J. Boyle, M.D., Associate Professor of Experimental Medicine, Wayne State University College of Medicine; Richard J. Bing, M.D., Professor and Chairman, Department of Medicine, Wayne State University College of Medicine; George W. Morley, M.D., Department of Obstetrics and Gynecology, University of Michigan Medical Center, Ann Arbor; D. Emerick Szilagyi, M.D., Department of Surgery, Henry Ford Hospital, Detroit; William N. Hubbard, M.D., Dean, University of Michigan College of Medicine, Ann Arbor.

In the afternoon, there will be section meetings for medical, surgical, and obstetrics and gynecology. General Chairman of the Annual Clinic Day is Eugene A. Otlewski, M.D.

Campaign for Freedom

(Continued from Page 1473)

next session of Congress, it will be our individual and collective obligation to:

1. As PATRIOTIC AMERICANS, stand for the cause of freedom against the tyranny of a new socialistic variety of social security.
2. As CITIZENS, participate in the national and state political campaigns to elect candidates who believe as we do, and to defeat candidates who are pledged to promote legislation which in our opinion would be detrimental to the best interests of our patients and our profession.
3. As DOCTORS OF MEDICINE, to convince our Senior citizens, and the public at large, that the best means whereby the aged can gain and maintain maximum health, and the optimum in medical care, is through adherence to and support of the progressive program for the care of the aged developed by the medical profession.

Every member of MSMS is urged also to use the new publications, which replaced the "Question of Freedom" pamphlet.

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Say you saw it in the Journal of the Michigan State Medical Society

Why diet is preferable to drugs ...in the control of serum

The objective of therapy is the approximation of the physiological norm.

This is most satisfactory when it can be accomplished by dietary manipulation. The control of elevated serum cholesterol through relatively simple changes in the dietary pattern of the patient puts nature's own processes to work most effectively to achieve the objectives of treatment.

The dietary approach does more than correct the serum cholesterol problem. Because overweight, together with improper eating patterns, is so often involved, the prescription of corrective diet helps the patient to help himself by establishing sound nutritional practices.

For the prophylaxis and prevention of hypercholestemia, the dietary approach affords the advantages of simplicity and economy. Diet therapy is for the long-term management of a chronic condition, while drug therapy is most efficient for acute situations.

The development of atherosclerosis is a slow process. It is believed that the onset of this condition is in early adulthood, but its clinical symptoms take as many as 20 years to manifest themselves. Simple changes in diet serve to keep the blood cholesterol concentration at an acceptable level.

Dietary therapy has other significant advantages over medication as follows:

1. Dietary adjustment involves little or no expense to the patient, whereas drugs are costly.
2. Dietary therapy may be made with complete safety—even for pregnant females.
3. Dietary therapy produces no side effects, whereas there is not as yet sufficient clinical evidence as to the long-term effects of drugs.
4. Dietary therapy brings about reduction in serum cholesterol through normal body processes, as yet not fully understood. On the other hand, some drugs can leave in the body accumulations of cholesterol precursors.
5. Dietary procedures do not usually generate new compounds in the blood which interfere with the chemical determination of blood serum cholesterol.
6. Dietary therapy offers a solution to the related problems of obesity which drugs do not.

Elevated serum cholesterol has long been linked to an imbalance in the ratio of the type of fat in the diet. Reductions in cholesterol levels have been achieved repeatedly, both in medical research and practice, through control of total calories and through replacement of an appreciable percentage of saturated fat by poly-unsaturated vegetable oil. An important measure in achieving replacement is the consistent use of poly-unsaturated pure vegetable oil in food preparation in place of saturated fat.

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Poly-unsaturated Wesson is unsurpassed by any readily available brand, where a vegetable (salad) oil is medically recommended for a cholesterol depressant regimen.

ROCK CORNISH GAME HENS—Free Wesson recipes for delicious main dishes, desserts and salad dressings are available for your patients. Request quantity needed from The Wesson People, Dept. N, 210 Baronne St., New Orleans 12, La.

More acceptable to patients. Wesson is preferred for its supreme delicacy of flavor, increasing the palatability of food without adding flavor of its own.

Uniformity you can depend on. Wesson has a poly-unsaturated content better than 50%. Only the lightest cottonseed oils of high iodine number are selected for Wesson, and no significant variations are permitted in the 22 exacting specifications required before bottling.

Economy. Wesson is consistently priced lower than the next largest seller.

Wesson's Important Constituents

Wesson is 100% cottonseed oil . . . winterized and of selected quality

Linoleic acid glycerides (poly-unsaturated)	50-55%
Oleic acid glycerides (mono-unsaturated)	16-20%
Total unsaturated	70-75%
Palmitic, stearic and myristic glycerides (saturated)	25-30%
Phytosterol (Predominantly beta sitosterol)	0.3-0.5%
Total tocopherols	0.09-0.12%

Never hydrogenated—completely salt free

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Squibb Announces Chemipen

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new chemically improved penicillin which provides the highest blood levels that are obtainable with oral penicillin therapy

As a pioneer and leader in penicillin therapy for more than a decade, Squibb is pleased to make Chemipen, a new chemically improved oral penicillin, available for clinical use.

With Chemipen it becomes possible as well as convenient for the physician to achieve and maintain higher blood levels—with greater speed—than those produced with comparable therapeutic doses of potassium penicillin V. In fact, Chemipen is shown to have a 2:1 superiority in producing peak blood levels over potassium penicillin V.*

Extreme solubility may contribute to the higher blood levels that are so notable with Chemipen.* Equally notable is the remarkable resistance to acid decomposition (Chemipen is stable at 37°C. at pH 2 to pH 3), which in turn makes possible the convenience of oral treatment.

And the economy for your patients will be of particular interest—Chemipen costs no more than comparable penicillin V preparations.

Dosage: Doses of 125 mg. (200,000 u.) or 250 mg. (400,000 u.), t.i.d., depending on the severity of the infection. The usual precautions must be carefully observed with Chemipen, as with all penicillins. Detailed information is available on request from the Professional Service Department.

Supply: Chemipen Tablets of 125 mg. (200,000 u.) and 250 mg. (400,000 u.), bottles of 24 tablets. Chemipen Syrup (cherry-mint flavored, nonalcoholic), 125 mg. per 5 cc., 60 cc. bottles.

*Knudsen, E. T., and Rolinson, G. N.: Lancet 2:1105 (Dec. 19) 1959.

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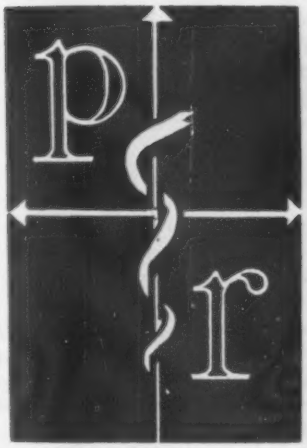
"As Others See Us"

By R. W. Teed, M.D., Chairman,

MSMS Public Relations Committee



PART I

REPORT OF AMA PUBLIC RELATIONS INSTITUTE

The two-day seminar opened in Chicago on September 1 with Leo Brown, Director of the AMA Communications Division, beginning the session. He said that in view of the recent discussion of the medical problems of aging, some people felt that the public was dissatisfied with medicine's efforts in this regard. However, he felt that this problem was selected for its emotional appeal and because politicians would like to transfer to themselves the image of "Protector of the Aged." They also are attempting to persuade the old folks to shift from personal responsibility to federal security, whatever that is.

He asked the question: "Are we communicating, or are we hiding our light?"

The object of the seminar was to answer that question.

* * *

THE KEYNOTE ADDRESS, "The Importance of the Public Image Versus Reality," was given by Pierre Martineau, Director of Research and Marketing, *Chicago Tribune*. He stated that people react to brand names rather than to the products themselves and that "image" is more important than reality. Many physicians believe that if we give the public the facts about medicine, people will believe our story. But the fact is that people exercise "receptive perception" and think in terms of cartoon or psychological images. This involves feeling or emotional reaction, and rationality seldom enters in. However, images can be modified, as was done by Chevrolet, Pepsi-Cola, menthol cigarettes, et cetera, without much recourse to facts. Medicine's problem is to present to the public a favorable image.

* * *

"HOW PEOPLE SEE DOCTORS" was presented by a panel consisting of an editor, a physician and a TV executive.

George Brandenburg, Midwest Editor of *Editor and Publisher*, Chicago, stated that, in his opinion, medical press relations were much better than they were 25 years ago, but further improvement was essential. Too many doctors are envious of their colleagues and collectively prevent them from telling the public what it wants to know. There is tremendous public interest in medicine, but due to a widespread policy of silence regarding the press, the public believes that medicine is a secret society. News stories about

medicine are valueless without names and places, and here, something has to give. Also, patients want to be told more about their illnesses, and to be allowed to co-operate in their treatment. The public frequently complains that doctors do not participate in community activities or assume civic responsibility, and activities of physicians in this regard should be portrayed. There is always a minority which dilutes the good done by the majority and distorts the image in the public mind. In giving a fair image we must avoid being phony.

Russell Roth, M.D., member of AMA Council on Medical Service, Erie, Pennsylvania, gave a physician's image of the physician. He is well trained, scientific and able to cope not only with the problems of medicine but also taxes, insurance forms, et cetera. He is not wealthy, but has a good home and status to maintain. His gross income is substantially reduced by overhead, taxes, contributions, etc. He is high on the list of fund-seekers, and usually contributes. He laments paperwork and regrets his ability to keep up with the literature. He will accept committee appointments but usually does little between meetings.

Herbert A. Carlborg, Director of Program Services for CBS TV, New York, stated that, as compared with other professions, the physician is high in TV circles, and is always placed in a favorable light. Actors and directors enjoy medical themes. The use of the "white coat" in drug advertising has been eliminated, and TV turns down millions in drug advertising. CBS employs a physician who meets with the medical directors of product companies and reviews their advertising claims. In general, Mr. Carlborg felt that the TV image of medicine is high.

* * *

"WHY PEOPLE SEE DOCTORS THAT WAY" was presented by a panel consisting of a sociologist, a medical cartoonist, and an insurance consultant.

Prof. Raymond Mack, Department of Sociology, Northwestern University, Evanston, Illinois, felt that the public's image of physicians was not entirely favorable. Medicine has not solved its problem by labelling the opposition as "socialists," and there are good reasons for many of our socialistic trends. Under the older, semi-feudal system, industries were small and people took care of each other, but under the present big industrial set-up, workers do not know each other, and the wage contract substitutes for individual help. Other contracts, such as unemployment benefits, social security, and other supplemental contracts bring the government into the picture. The laboring public believes these are essential, and if medicine objects it is labelled reactionary.

Nicholas Dallis, M.D., creator of the comic strip "Rex Morgan, M.D.," Scottsdale, Arizona, believes that the public would like a doctor with the image of Jesus Christ who would "lay hands on them" and heal them. The conscious image of the public has slipped from that of a physician whose word is law to one who is questioned. Twenty-five years ago, few medical students married, but this has changed, and by the time the average physician enters practice, he has been married several years and has children. This means he has learned to be a business man and collects his bills better, which has not improved the public's image. Also, drugs have improved therapy so much that the physician does not spend as much time with the patient as formerly, and hence has less time to influence the patient.

James E. Bryan, consultant, Medical Administration and Medical Care Prepayment, Stanford, Connecticut, believes that contemplating our image can be an escape device so that we do nothing about reality. Every group has an "interior" image which is its own, and an "exterior" image which is that of the public. The nature of the mission of medicine has produced an image of nobility, which was greater in the days when the physician had to struggle with disease more or less alone. Today, drugs have changed this, and the personality of the patient has become eclipsed, regrettably. The public image of medicine is ambivalent, since on the one hand there is awe of science, but on the other hand there is fear that a Frankenstein may eventually take over. Medicine must realize that treatment, for the patient, is a right, and unite with sociology, chemistry, bacteriology, pharmacology and pathology to give the public all the benefits of modern knowledge.

* * *

AT THE LUNCHEON, Ernest B. Howard, M.D., Assistant Executive Vice President of AMA, spoke on "The Political Outlook," and stated that Senator Kennedy has been pushed into the doctrinaire position that the old folks must be made wards of the government, regardless of their wishes in this regard, although his own party has rejected this position. He stated that Blue Cross needs overhauling, since some officials have approved of the Social Security approach, and none took a strong, unequivocal position against the Forand Bill. Certain businesses likewise approved a payroll deduction because this reduced income and corporation taxes. Medicine lost the press in the recent campaign, and labor succeeded in creating the impression that there was a crisis which could only be managed by governmental action. The press uniformly predicted the passage of the Forand Bill. Medicine's view, that the aged are not in a total position of indigency, must be presented at the coming White House Conference. The AMA favors the Mills Bill because it believes this bill answers the problem.

(Part II of the Report will appear next month.)

(Continued on Page 1486)

SAUNDERS BOOKS

New (12th) Edition!—Thoroughly Revised and Up-to-Date

Greenhill—Obstetrics

This beautifully illustrated volume, in a completely revised edition, covers virtually every aspect of obstetrics *from nutritional counseling of the mother in early stages of pregnancy to pathology of the newborn.* Dr. Greenhill and his collaborators fully explain the mechanisms of labor plus step-by-step procedures in delivery. Effective care at every stage is detailed—immediate treatment of unexpected difficulties; prevention of accident and infection; relief of discomfort; management of various disease states concurrent with pregnancy. Complications and pitfalls are well outlined. The authors bring you fuller understanding of such topics as: *Antepartum Care—Toxemias of Pregnancy—Abortion—Multiple Pregnancy—Effects of Labor on the Child—Breech Extraction—Etc.*

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A New Book!—Useful Techniques for Interpreting Chest Roentgenograms

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This practical text presents a clear introduction to x-ray diagnosis by demonstrating many useful techniques for interpreting chest films. It deals primarily with fundamentals and considers specific disease entities only for the purpose of illustrating the principles discussed. Many beautifully reproduced roentgenograms augment and illuminate the text discussions. An extensive series of films of normal chests shows minor deviations from the normal picture and explains which can be safely ignored. In addition, Dr. Felson includes a separate chapter on special roentgen signs which have important diagnostic implications. Here you will find *The Pulmonary Meniscus Sign, The Double Lesion Sign, The Notch Sign, The Butterfly Shadow, The Sail Shadow of the Thymus, etc.* The principles outlined here can be effectively applied to evaluation of films of other body areas.

By BENJAMIN FELSON, M.D., Professor and Director, Department of Radiology, University of Cincinnati College of Medicine; Director, Department of Radiology, Cincinnati General, Children's, Daniel Drake, Dunham, Christian R. Holmes, and Longview Hospitals; Special Consultant, U. S. Public Health Service; Consultant to the Dayton and Cincinnati Veterans Administration Hospitals. 301 pages, 6½"x10", with 450 illustrations on 238 figures. About $11.00. *New—Just Ready!*

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Johnstone & Miller—Occupational Diseases & Industrial Medicine

With increased exposure of the public to toxic materials, more physicians are confronted with situations closely related to the practice of industrial medicine. This useful volume compiles all the known information about occupational disorders—*their prevention, diagnosis and management.* The authors illuminate the full spectrum of the field from *Scope and Elements of Industrial Medical Practice* to *Diagnosis of Occupational Diseases.* The major part of the book is devoted to clear, concise descriptions of the occupational diseases, utilizing the clinical approach throughout. Organization logically progresses from etiology, signs and symptoms, treatment, estimation of permanent and temporary disability. Treatment is well outlined. Among the injurious agents covered, you'll find *Noxious Gases, Resins and Plastics, Pesticides, Ionizing Radiations, etc.*

By RUTHERFORD T. JOHNSTONE, M. D., Consultant in Industrial Medicine, Clinical Professor of Preventive Medicine and Public Health and Clinical Professor of Medicine, University of California at Los Angeles; and SEWARD E. MILLER, M.D., Director, Institute of Industrial Health, Professor of Medicine, Medical School, Professor of Industrial Health, School of Public Health, University of Michigan, Ann Arbor. 482 pages, 6¼"x9¾", illustrated. About $11.50. *New—Just Ready!*

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MSMS Distributes Message In State Fair Exhibit

MSMS presented an educational exhibit in Detroit in September at the Michigan State Fair, where thousands of fair visitors were given a printed message from the Michigan State Medical Society.

The message, which follows, warned against "any intrusion of unnecessary governmental controls to hamper your doctor:"

"You and your doctor are partners in good medical care just as the Michigan State Medical Society and the general public are partners in maintaining high standards of health in Michigan. Both your doctor and his organization welcome your suggestions and constructive criticisms.

"This is voluntary, friendly cooperation that has given Michigan people the best medical care in the world. This same kind of mutual understanding will assure the necessary progress to maintain this life-giving, life-saving, superiority in medical service.

"Any intrusion of unnecessary governmental controls is a hampering thing to your doctor. It can cause embarrassment and loss of privacy to you when you are a doctor's patient. Less service, slower progress, is the inevitable result.

"Yet some politicians are trying to get elected by promising to give you government medical service! They want to increase your social security taxes and then, instead of repaying this money to you when you become eligible to receive social security benefits, they want to pay you off with certain services, at certain times, at certain places from government doctors.

"Let's keep medical care a partnership between you and your own private doctor.

"Express your feeling in this regard at the General Election this November when those candidates for national offices espousing the idea of increasing your social security taxes and giving you second-rate government medical services in return, ask for your vote."

Seek Solutions to Complex Matter

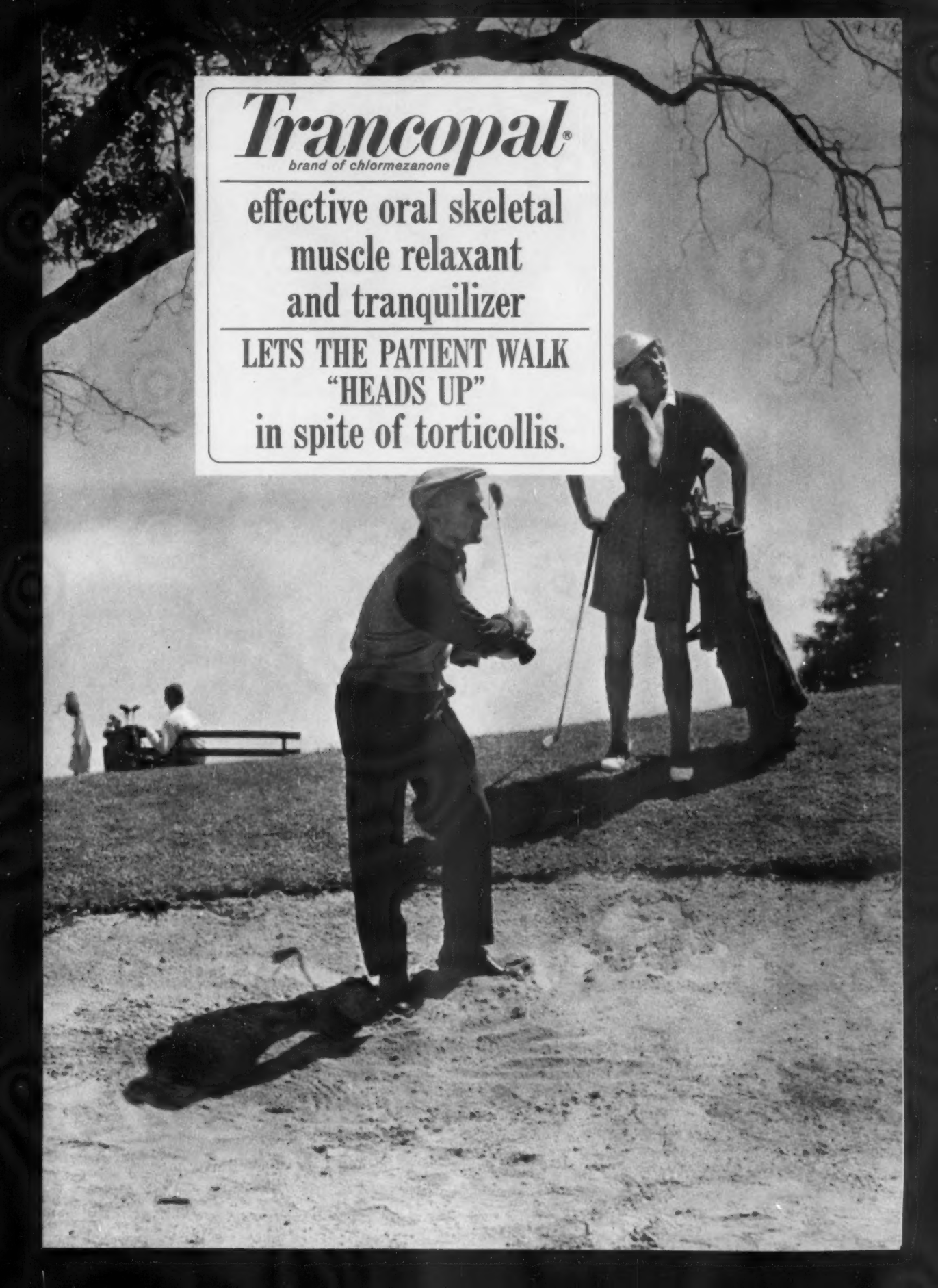
No group is more intimately concerned with problems of the aging than the members of the medical profession. Nor, in all likelihood, has any group devoted more study to the aging process or worked harder to find solutions to the many problems that accompany it.

The one thing that stands out in any study of the aged is that their problems are far broader than those of health alone. The aged have special needs in the field of housing, in recreation, in finding acceptance and understanding within the community, in the effort to be useful, in the preparation for retirement.

Appeal to Students

Dean William N. Hubbard, M.D., and other U-M faculty members presented a "Health Careers Night" program for the students at Ann Arbor High School this spring. Dr. Hubbard and his group met with students interested in careers in the field of medicine.

Say you saw it in the Journal of the Michigan State Medical Society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effective oral skeletal
muscle relaxant
and tranquilizer
LETS THE PATIENT WALK
"HEADS UP"
in spite of torticollis.

Trancopal

relieves pain and spasm associated with torticollis.

In a recent study by Ganz, Trancopal brought considerable improvement or very effective relief to 20 of 29 patients with torticollis.[1] "The patients helped by the drug," states Ganz, "were able to carry the head in the normal position without pain." Similarly, Kearney found that in 8 of 13 patients with chronic torticollis treated with Trancopal improvement was excellent to good. ". . . Trancopal is the most effective oral skeletal muscle relaxant and mild tranquilizer currently available."[2]

Lichtman, in a study of patients with various musculoskeletal conditions, noted that 64 of 70 patients with torticollis obtained excellent to good relief with Trancopal.[3]

In a comparative study of four central nervous system relaxants, Lichtman reports that 26 of 40 patients found Trancopal to be the most effective drug.[3]

1. Ganz, S. E.: *J. Indiana M. A.* 52:1134, July, 1959. 2. Kearney, R. D.: *Current Therap. Res.* 2:127, April, 1960. 3. Lichtman, A. L.: *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958.

Trancopal (brand of chlormezanone) and Caplets, trademarks reg. U. S. Pat. Off. 4716

Clinical results with *Trancopal*®[2]

	Excellent	Good	Fair	Poor	Total
LOW BACK SYNDROMES					
Acute low back strain	25	19	8	6	58
Chronic low back strain	11	5	1	1	18
"Porters' syndrome"*	21	5	1	1	28
Pelvic fractures	2	1	—	—	3
NECK SYNDROMES					
Whiplash injuries	12	6	2	1	21
Torticollis, chronic	6	2	3	2	13
OTHER MUSCLE SPASM					
Spasm related to trauma	15	6	1	—	22
Rheumatoid arthritis	—	18	2	1	21
Bursitis	2	6	1	—	9
TENSION STATES	18	2	4	3	27
TOTALS	112 (51%)	70 (32%)	23 (10%)	15 (7%)	220 (100%)

*Over-reaching in lifting heavy bags resulting in sprain of upper, middle, and lower back muscles.

Dosage: **Adults, 200 or 100 mg. orally three or four times daily.**
Relief of symptoms occurs in from fifteen to thirty minutes and lasts from four to six hours.

How Supplied: Trancopal Caplets®
200 mg. (green colored, scored), bottles of 100.
100 mg. (peach colored, scored), bottles of 100.

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(phenoxyethyl penicillin potassium)

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Complete information on indications, dosage and precautions is included in the circular accompanying each package.

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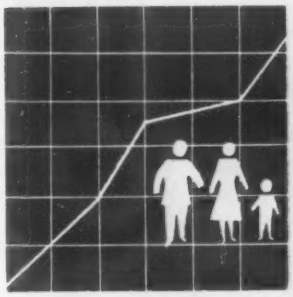
ACUTE PHARYNGITIS	SYNCILLIN® 500 mg. t.i.d. - 5 days
W. M. 24-year-old-male. Admitted with sore throat which had progressed rapidly in severity for 24 hrs. Temp. 104.4. Pulse 110. Acute pharyngitis and enlarged, red, bulging tonsils covered with pus. Throat culture revealed beta hemolytic strep. Patient given 500 mg. SYNCILLIN t.i.d. Within 24 hrs., fever terminated by crisis with marked relief of local signs and symptoms. After 5 days, infection was cured.	

Actual case summary from the files of Bristol Laboratories' Medical Department

State M.D.'s Contribute To Medical Colleges



The American Medical Education Foundation has issued the following information about physician support to medical schools during 1959.

The report shows that the University of Michigan received a total of $49,621 from 1,279 contributors; and Wayne State University received $17,616 from 360 contributors. AMEF points out that the total of "contributions" could also be labeled "number of contributions" because many doctors gave both to their schools and to AMEF or to several schools.

The annual report also shows that in Michigan, 623 contributions were made to AMEF and 1,692 by alumni, with these contributions totaling $18,736 to AMEF and $80,117 to alma maters for a total of $98,853.

The funds will be used by the medical schools for teaching, building funds, research, scholarships, library and other purposes.

Benefits Set Faster Pace

Benefits paid to persons covered by hospital expense insurance are increasing at a much faster pace than the number of persons with such insurance, the Health Insurance Institute reports.

From 1958 to 1959, the rate of increase in hospitalization benefits was triple that of persons with hospital insurance, said the Institute, while from 1952 through 1959 the growth rate of benefits was quadruple that of persons covered.

The number of persons covered by hospital expense insurance provided by insurance companies, Blue Cross-Blue Shield, and other health care plans rose from 123,038,000 at the end of 1958 to 127,896,000 at the end of 1959, an increase of 3.9 per cent.

At the same time, benefits to pay for the costs of hospital care climbed from $2,589,000,000 in 1958 to $2,904,000,000 in 1959, a boost of 12.2 per cent, and more than triple the rate of increase in coverage, according to the Institute.

More than Half of Federal Workers Enroll in Blue Cross-Blue Shield

Blue Cross-Blue Shield led all other organizations in the enrollment of federal workers who became eligible for coverage under the Federal Employee Health Benefits legislation enacted last year.

More than 55 per cent of the estimated 1,695,000 federal workers who selected health benefits coverage from among the 38 programs available chose to enroll in Blue Cross-Blue Shield.

Nearly complete tabulations of the distribution of enrollment between the various programs which were released by the Civil Service Commission in late July indicated that enrollment in Blue Cross-Blue Shield was more than twice as large as enrollment in the government-wide indemnity benefits program provided through the Aetna Life Insurance Company. All other programs, including those offered by government employee and group health organizations, accounted for but 19 per cent of the total enrollment, or approximately 325,000 enrollees.

The breakdown of enrollment totals showed that government employees chose the high level-higher cost benefits program in preference to the low benefit-lower cost option offered by Blue Cross-Blue Shield in a ratio of about four to one.

The choice exercised by federal employees in selecting health benefits programs is described by Blue Cross and Blue Shield association officials as especially significant because it was the first time the element of free choice involving such a variety of programs has been exercised by so many individuals at one time.

Number of Persons Covered by Health Insurance in USA Continues to Increase

Seventy-two per cent of the civilian population—or more than 127 million Americans—had health insurance at the end of 1959. This figure is based on reports from insurance companies, Blue Cross-Blue Shield and other health care plans.

Both the number of persons covered by health insurance and the amount of benefits paid reached new highs last year. Coverage increased by 4.8 million during 1959 to reach a total of 127,896,000 persons with health insurance protection. Benefit payments by all health insuring organizations amounted in 1959 to more than $4.3 billion, up $400 million over 1958.

In addition, persons with loss-of-income policies received $838 million in benefits from insurance companies to replace income lost through disability. Thus, a grand total of $5,175,000,000 in health insurance benefits were distributed during 1959, up 10.9 per cent over 1958.

Hospital expense insurance was provided by insurance companies to 75,457,000 persons; by Blue Cross-Blue Shield and similar groups to 56,825,000 and by other health care plans to 4,861,000.

Surgical expense insurance by insurance companies covered 72,263,000 persons; by Blue Cross-Blue Shield and similar groups 48,843,000, and by others 5,813,000.

Regular medical expense insurance accounted for 42,999,000 persons through Blue Cross-Blue Shield and similar groups; 38,227,000 through insurance company programs, and 6,347,000 through other plans.

Says Public Needs to Understand Why Hospital Costs Will Jump in Decade

Public understanding of the need for raising health insurance costs in view of conservative estimates that hospital costs will increase by 50 per cent during the next decade was urged in a study by the Columbia University School of Public Health and Administrative Medicine on Blue Cross Plans in New York State.

The study, begun in 1958 under the direction of Ray E. Trussell, Professor of Administrative Medicine, was commissioned by the New York State Health and Insurance Departments in an effort to resolve some of the problems relating to nonprofit health insurance here. Among the recommendations of the study are:

Coverage by Blue Cross of outpatient services.

Greater participation by labor, industry, and the general public in Blue Cross management.

A uniform state-wide basic contract.

Abandonment of the principle of experience rating in determining coverage costs.

Blue Cross payments only to accredited hospitals.

Compare Salient Points in CHA Plan, and Blue Shield-Blue Cross

A comparison of the Community Health Association prepaid medical and hospital plan and Blue Shield-Blue Cross was sent recently to the presidents, secretaries and editors of the component societies of Michigan and also to the members of The MSMS Council.

The covering letter, in part, stated:

"Labor's social planners, under CHA's Executive Director F. D. Mott, M.D., have designed a program to offer essentially the same hospital benefits now available through Blue Cross but are projecting a "pilot program" which on the surface appears to have some broader medical care benefits than those of Blue Shield. CHA's rates are slightly higher than the Blues.

"CHA, which hopes to begin operations January 1, 1961, has announced that it expects to be able to take care of about 70,000 persons within a year. It will make its services available to any Metropolitan area group with a "common employer." The present

(Continued on Page 1494)

after milk and rest, why Donnalate?

Once you've prescribed milk and rest for a peptic ulcer patient, Donnalate may be the best means for fulfilling his therapeutic regimen. This is because Donnalate combines several recognized agents which effectively complement each other and help promote your basic plan for therapy. A single tablet also simplifies medicine-taking.

in Donnalate: Dihydroxyaluminum aminoacetate affords more consistent neutralization than can diet alone. • Phenobarbital improves the possibility of your patient's resting as you told him to. • Belladonna alkaloids reduce GI spasm and gastric secretion. And by decreasing gastric peristalsis, they enable the antacid to remain in the stomach longer.

Each Donnalate tablet equals one Robalate® tablet plus one-half Donnatal® tablet: Dihydroxyaluminum aminoacetate, N. F., 0.5 Gm.; Phenobarbital (1/8 gr.), 8.1 mg.; Hyoscyamine sulfate, 0.0519 mg.; Atropine sulfate, 0.0097 mg.; Hyoscine hydrobromide, 0.0033 mg.

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(Continued from Page 1492)

area of endeavor will be Wayne, Oakland, Macomb, Washtenaw, and Monroe Counties.

"CHA literature states: Each CHA member selects his own doctor from a medical group. Presently, CHA has under contract only Metropolitan Hospital, 1800 Tuxedo Avenue, Detroit, with 110 beds and 18 full-time MDs on its staff. Except in an emergency, all CHA members must go to this institution for care and be treated by a panel of only 18 doctors. CHA plans to build up the program as quickly as facilities (hospitals and doctors in group medical practice) can be signed up.

"CHA is a non-profit *cooperative* headed by UAW President Walter P. Reuther. It is not incorporated under the acts which cover Blue Cross and Blue Shield and, therefore, does not come under the State Insurance Commissioner.

"The Big Three employer-union agreements of 1958 provide that the CHA-type program may be offered to employees who could choose it or Blue Cross-Blue Shield or a commercial insurance company plan. Accordingly, UAW will seek conferences with the Big Three auto companies to offer its plan. Over 500,000 auto plant and allied workers are now covered by Blue Cross-Blue Shield with employees paying half the cost of coverage for themselves and their dependents while the company pays the other half."

SALIENT POINTS OF BLUE CROSS-SHIELD BENEFITS VS COMMUNITY HEALTH ASSOCIATION PROPOSALS

Blue Cross-Blue Shield	*Community Health Association*
1. Subscribers may choose their own doctor and almost any hospital in Michigan.	1. CHA members must go to Metropolitan Hospital in Detroit and be treated by a panel of available CHA doctors, except in emergencies.
2. Up to 120 days (semi-private basis) in the hospital, with non-eligible period of 90 days between hospital stays.	2. Same.
3. Complete surgical and medical care in the hospital, plus drugs, medicines, and laboratory services for hospital patients.	3. Same
4. Office calls are not as yet included in the Blue Shield program.	4. CHA will pay for office calls, the member paying $1. per visit except for immunization, lab. service, or physiotherapy.
5. Home calls are not as yet included in the Blue Shield program.	5. CHA will pay for home calls by doctors but only in a prescribed area (Detroit, part of Dearborn, Hamtramck, and Highland Park). A fee is charged for the first visit ($4.00 by day and $6.00 by night) but subsequent visits for same medical condition are free.
6. Blue Cross is experimenting with a home nursing service plan but it is not yet offered generally.	6. CHA will pay for up to 60 days of home nursing services in a prescribed area (Detroit, part of Dearborn, Hamtramck, and Highland Park).
7. Blue Shield covers surgery and emergency first aid in the doctor's office.	7. CHA will pay for all services in the doctor's office, including routine care.
8. As yet, Blue Shield does not include preventive medicine in its program.	8. CHA will pay for periodic physical examinations, pediatric care, injections, and vaccinations.
9. Blue Cross-Blue Shield pay for diagnostic x-rays, electrocardiograms, laboratory tests, and x-ray treatments, with a minor part of the costs being paid by subscribers.	9. CHA will pay for these diagnostic services.
10. Blue Cross-Blue Shield pay for maternity care after a nine-month waiting period.	10. CHA pays for maternity care before, during, and after birth with no waiting period.
11. Blue Shield as yet does not include eye examinations.	11. CHA will pay for eye examinations.
12. Blue Cross-Blue Shield do not pay for eye glasses, dental care, ambulance service, blood, or drugs and medicine for non-hospitalized patients.	12. Same.

RATES

Blue Cross-Blue Shield—Plan B

Individual Income	*Family Income*
$ 6.78	$ 7.49
16.52	18.27
17.74	20.08

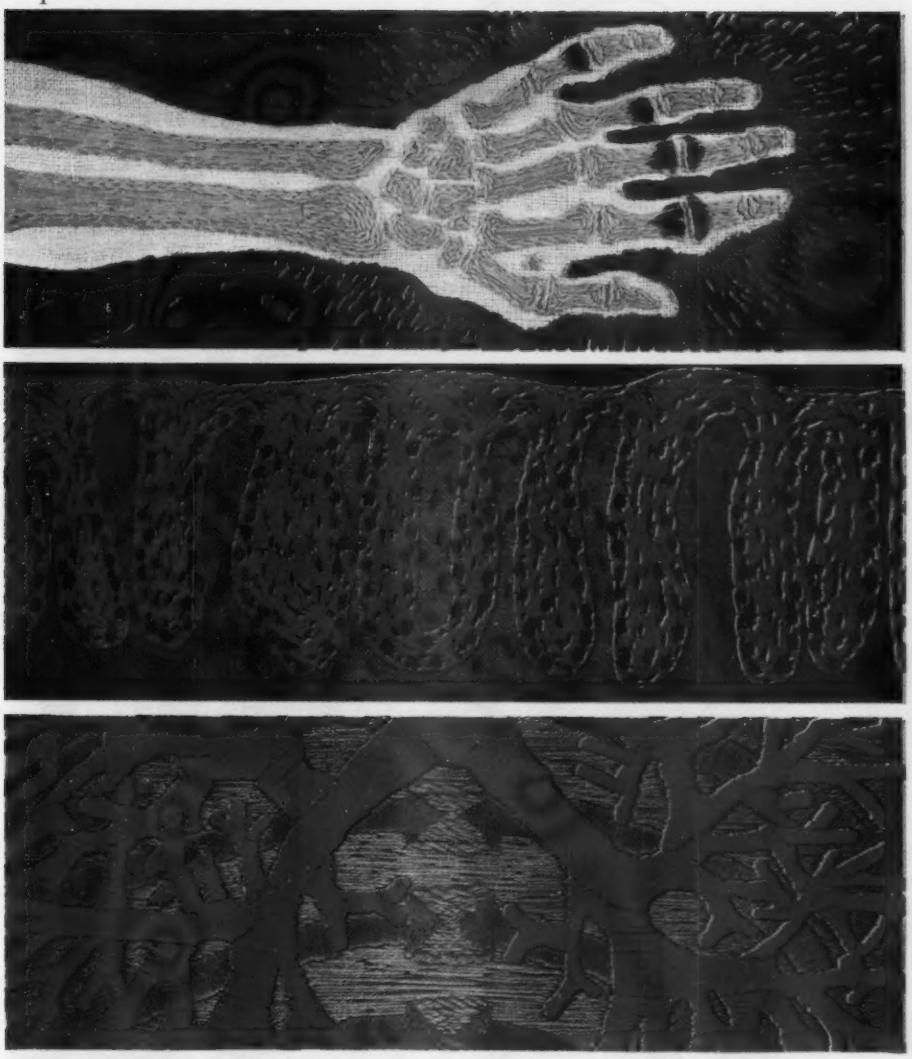
Community Health Association

Flat rate, regardless of family income

Single subscriber	$ 8.00
Couple	18.80
Family	20.60

CHA subscribers pay $1.00 fee for each visit to OPD; also $4.00 for first house call and $6.00 for first night call per illness (available in a limited geographic area).

a promise fulfilled



All corticosteroids provide symptomatic control in rheumatoid arthritis, inflammatory dermatoses, and bronchial asthma. They *differ* in the frequency and severity of side effects. Introduced in 1958, ARISTOCORT Triamcinolone bore the promise of high efficacy and relative safety. Physicians today recognize that the promise has been fulfilled . . . as evidenced by the high rate of refilled ARISTOCORT prescriptions.

Aristocort Triamcinolone LEDERLE

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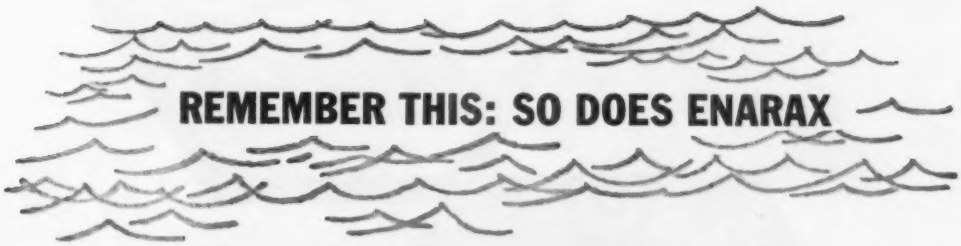
WHEN ULCEROGENIC FACTORS KEEP ON WORKING...

Say you saw it in the Journal of the Michigan State Medical Society



REMEMBER THIS: SO DOES ENARAX

Think of your patient with peptic ulcer—or with gastrointestinal dysfunction—on a typical day.

Think of the anxieties, the tensions.

Think, too, of the night: the state of his stomach emptied of food.

Disturbing?

Then think of ENARAX. For ENARAX was formulated to help you control precisely this clinical picture. ENARAX provides oxyphencyclimine, the inherently long-acting anticholinergic (up to 9 hours of actual achlorhydria[1]) . . . plus Atarax, the tranquilizer that doesn't stimulate gastric secretion.

Thus, with b.i.d. dosage, you provide continuous antisecretory/antispasmodic action **and** safely alleviate anxiety . . . with these results: ENARAX has been proved effective in 92% of G.I. patients.[2-4]

When ulcerogenic factors seem to work against you, let ENARAX work for you.

ENARAX® B.I.D.

(10 MG. OXYPHENCYCLIMINE PLUS 25 MG. ATARAX®†) A SENTRY FOR THE G.I. TRACT

dosage: Begin with one-half tablet b.i.d.—preferably in the morning and before retiring. Increase dosage to one tablet b.i.d. if necessary, and adjust maintenance dose according to therapeutic response. Use with caution in patients with prostatic hypertrophy and only with ophthalmological supervision in glaucoma.

supplied: In bottles of 60 black-and-white scored tablets. Prescription only.

References: 1. Steigmann, F., **et al.:** Am. J. Gastroenterol. 33:109 (Jan.) 1960. 2. Hock, C. W.: to be published. 3. Leming, B. H., Jr.: Clin. Med. 6:423 (Mar.) 1959. 4. Data in Roerig Medical Department Files.

†brand of hydroxyzine

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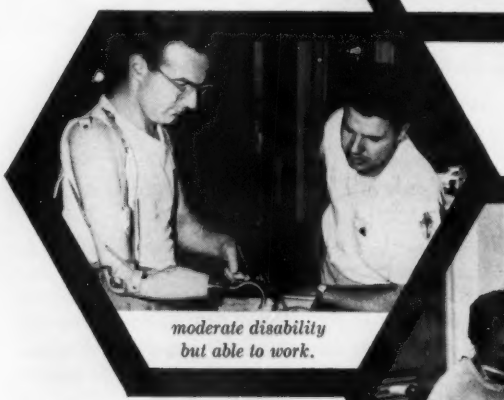

moderate disability but able to work.

severely disabled but not totally incapacitated.

...through comprehensive rehabilitation for

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- amputations
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- traumatic disabilities of the hand
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Services Available for both in and out patients:

- Medical Care
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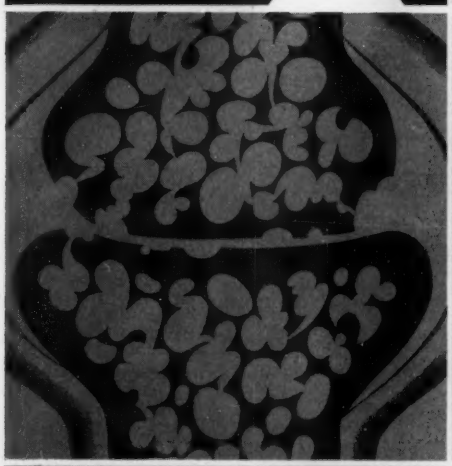

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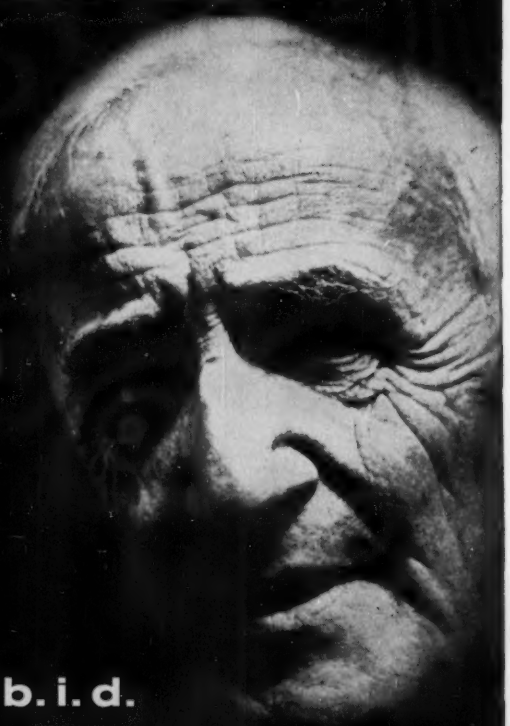

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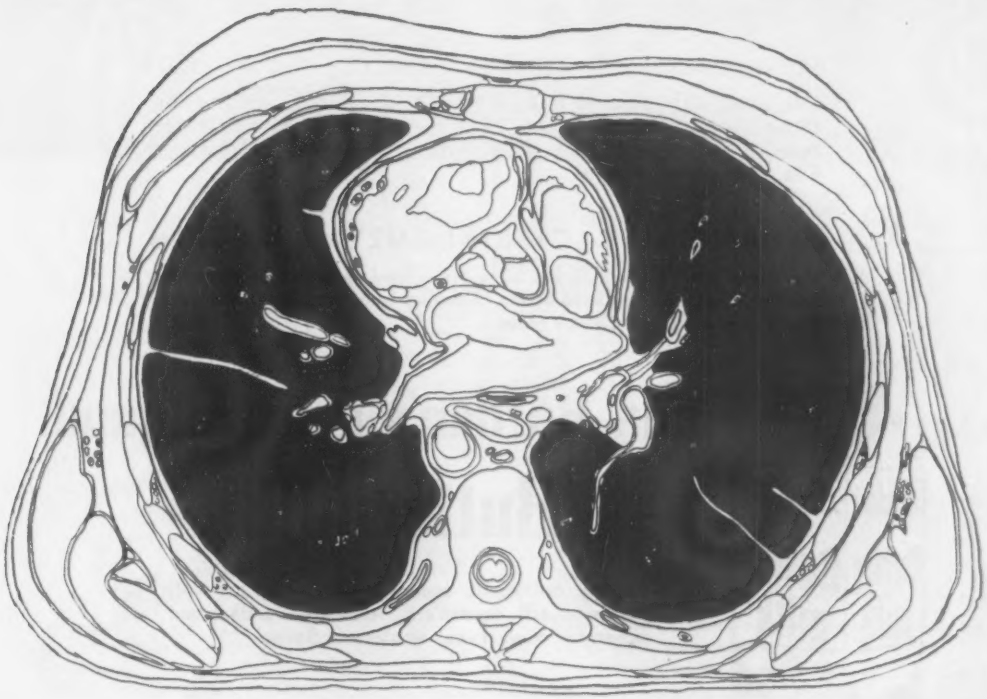

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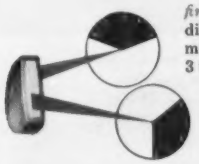

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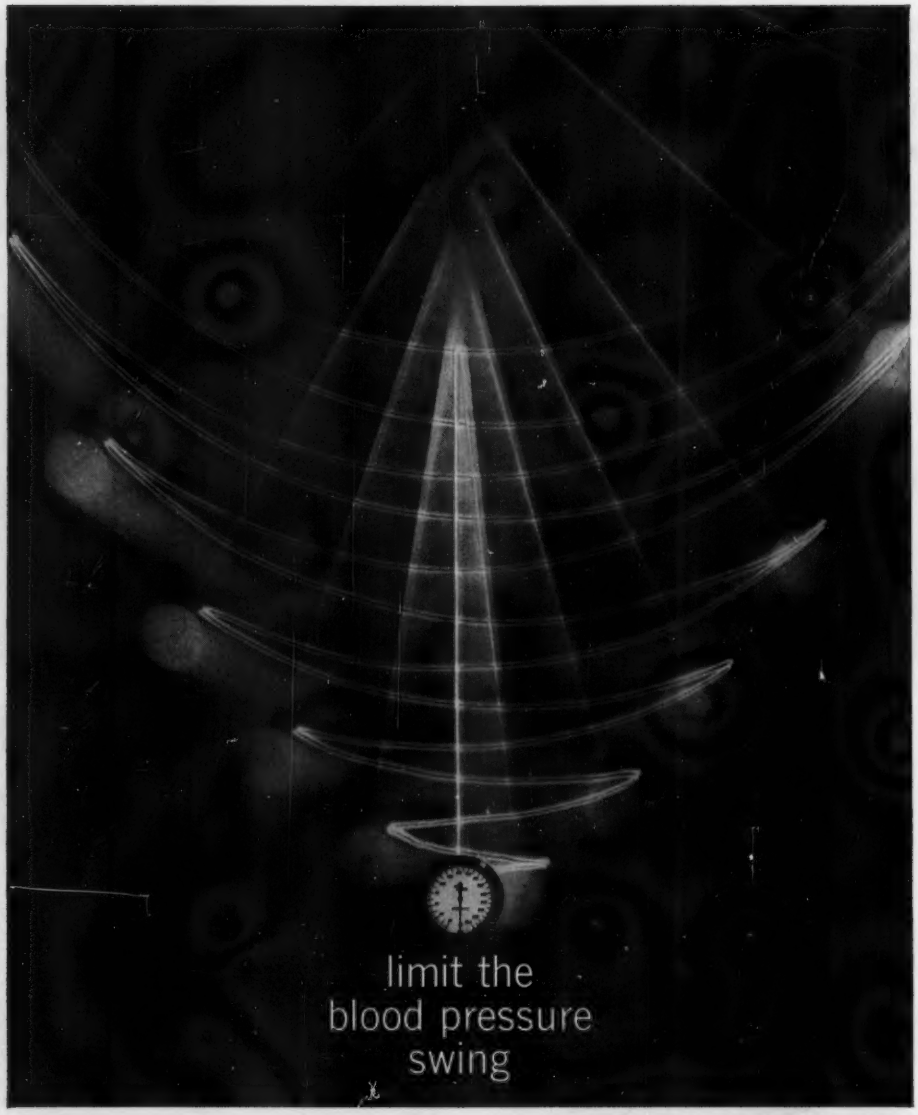

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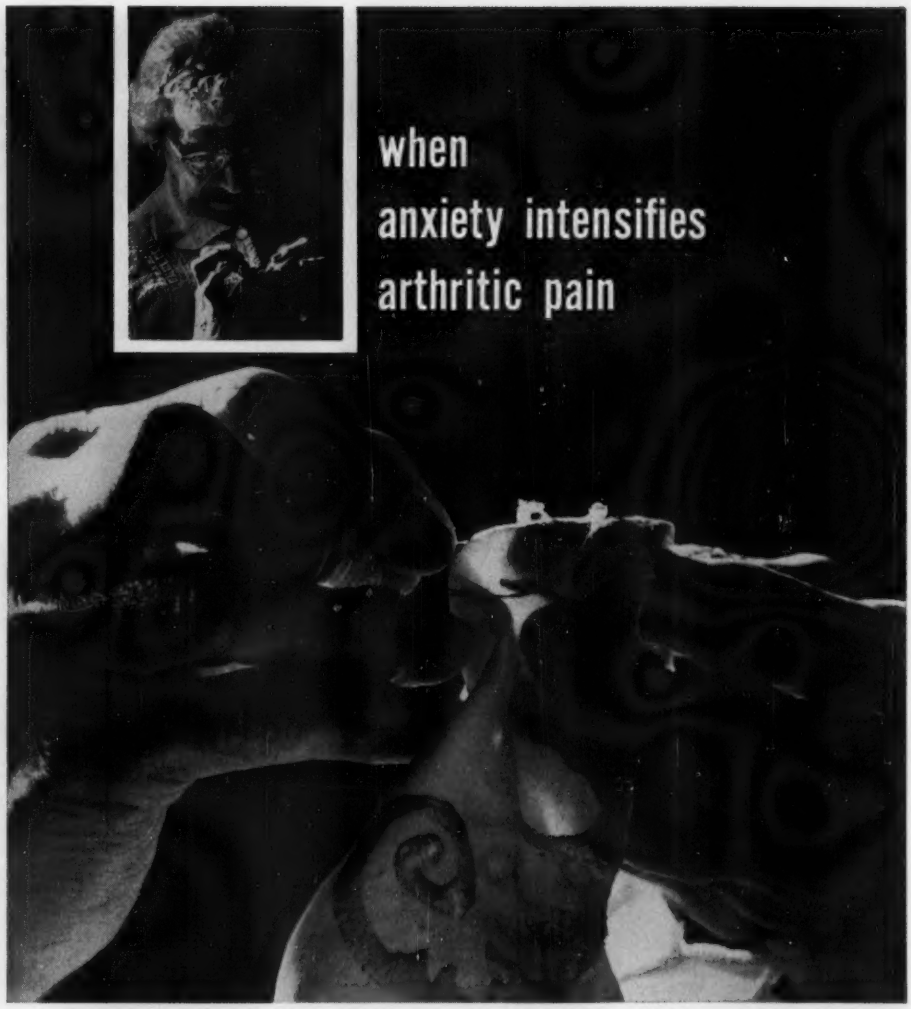

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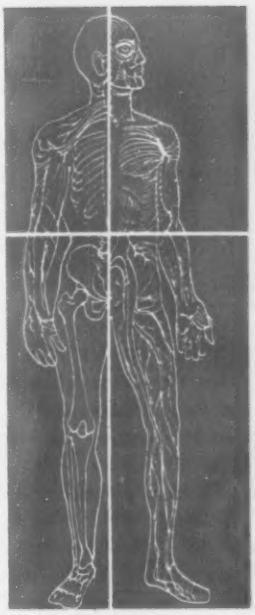
Insulin, Diabetes and Adipose Tissue

A *Brief Review*

George F. Cahill, Jr., M.D.
Boston, Massachusetts



KNOWLEDGE of the physiology of diabetes and insulin has increased irregularly since the isolation of the active pancreatic principle by Banting and Best in 1921.[1] Their report was soon followed by a series of experiments demonstrating that insulin directly increases glucose removal by peripheral tissues.[2,3] The succeeding two decades witnessed major developments in the treatment of clinical diabetes such as the use of long-acting insulin preparations; however, with the exception of the demonstration of the turnover of body constituents by Schoenheimer[4] followed by application of these techniques to the diabetic by Stetten,[5] there were few major advances in the basic understanding of the disease.

In the mid 1940's, Cori and his collaborators suggested that insulin primarily altered the activity of hexokinase, the enzyme catalyzing the entry of glucose into the metabolic pool of hexose phosphates.[6,7] Opposition to this concept of insulin action soon developed, particularly when several laboratories[8-10] were unable to find the expected decreased levels of this enzyme in diabetic tissues to account for the observed decrease in glucose metabolism. Several years later, Levine and his coworkers,[11,12] suggested that insulin primarily effected an increased permeability of the cell membrane to glucose, using the galactose space in hepatectomized dogs as a model system. Ross,[13] working independently in the Institute of Ophthalmology, London, likewise came to the same conclusion studying the penetration of various substances into the lens.

During this period, attention was primarily directed to muscle and liver metabolism, probably due to the convenience of the rat diaphragm and the liver slice as laboratory preparations. Nevertheless, certain investigators, notably Wertheimer and Shapiro[14] in Jerusalem, and Hausberger[15] and Renold[16] in this country, were drawing attention to the metabolic lability of adipose tissue, particularly in respect to its apparent response to insulin and diet.

From the Departments of Medicine, Harvard Medical School and the Peter Bent Brigham Hospital, Boston, Massachusetts.

Dr. Cahill is a Fellow of the Medical Foundation, Inc., Boston, Massachusetts.

Supported in part by a grant from the U. S. Public Health Service (H-4569), Bethesda, Maryland.

Mechanism of Insulin Action

In the past five years, the basic concepts which had been previously considered firm have undergone considerable revision. One exception is the Levine hypothesis, which has since been confirmed and expanded. Using the perfused heart as a model, Park, Morgan and their collaborators[17-19] have shown that insulin primarily facilitates the ease whereby carbohydrates of certain structure—obviously including glucose—are allowed to penetrate the heart muscle wall into the intracellular fluid. The enzyme hexokinase is then available to further metabolize the carbohydrate if it is a substrate for the enzyme (the enzyme has its own pattern of structural specificity). This insulin effect is not merely the opening of pores in the cell wall, (1) since it is structurally specific for certain carbohydrates as stated above, (2) since certain sugars compete with one another for entry suggesting binding to a "carrier" mechanism, and (3) since the mechanism conforms to mathematical quantitation similar to that of an enzymatic system.[17]

Muscle was generally accepted as the tissue primarily affected by insulin, as reflected by increased glucose uptake and conversion to and storage as glycogen. In addition, it was considered that in the animal with adequate insulin reserves, a certain proportion of the carbohydrate was converted to lipid in the liver (it had been well-established that fatty acid synthesis in liver from diabetic animals was markedly decreased, and that insulin-treatment of the animal returned this capacity to normal). The lipid was then thought to be transported to peripheral fat depots and stored as such until times of need.

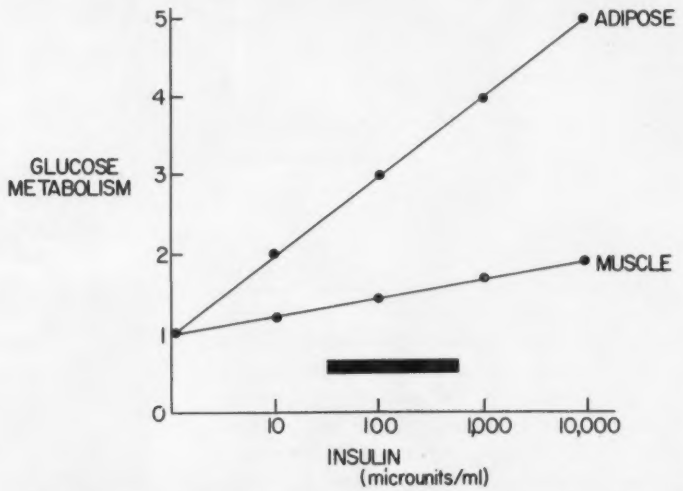


Fig. 1. Comparison of effect of insulin concentration on glucose metabolism in adipose tissue and muscle. The approximate concentrations of insulin in serum are covered by the range of the dark bar. Values for glucose uptake are in arbitrary units.

Adipose Tissue, the Primary Site of Insulin Action

The work of several investigators, particularly that of Favarger[20] and his group in France, has shown that lipogenesis (synthesis of fatty acids from carbohydrate) occurs directly in adipose tissue itself, and that perhaps nine-tenths or more of fatty acids synthesized from carbohydrate are synthesized in the adipose cell and not in liver or other tissues. In a parallel vein, Renold and his group[21-26] in Boston, have demonstrated an exquisite role played by insulin in the regulation of glucose metabolism and lipogenesis in adipose tissue. Their *in vitro* experiments have shown that this tissue responds to insulin by a dramatic acceleration of glucose metabolism, primarily resulting in conversion of glucose to fatty acids and storage of these as triglycerides. Not only is the degree of the response startling, but in addition, the concentration of insulin able to effect this alteration in metabolism is extremely small, in the order of 5 microunits/milliliter or less (Fig. 1). Thus, adipose tissue appears not only to be the most dramatically altered tissue in the presence of insulin, but may respond to lesser quantities of insulin when compared to other tissues. Extrapolating from these facts, it might be inferred that adipose tissue is the principal

site of insulin action. In addition, its response to concentrations of insulin as small as 5 microunits/milliliter, far less than the smallest estimates of the concentration of insulin in human sera, suggest that insulin continuously exerts an effect on adipose tissue and its metabolism of glucose.

Mechanism of Free Fatty Acid Release

Recent experiments have shown that triglycerides in adipose tissue are continuously split to form intracellular free fatty acids and glycerol.[22,23] The glycerol is apparently released into the circulation and metabolized to glucose by liver, which has the necessary

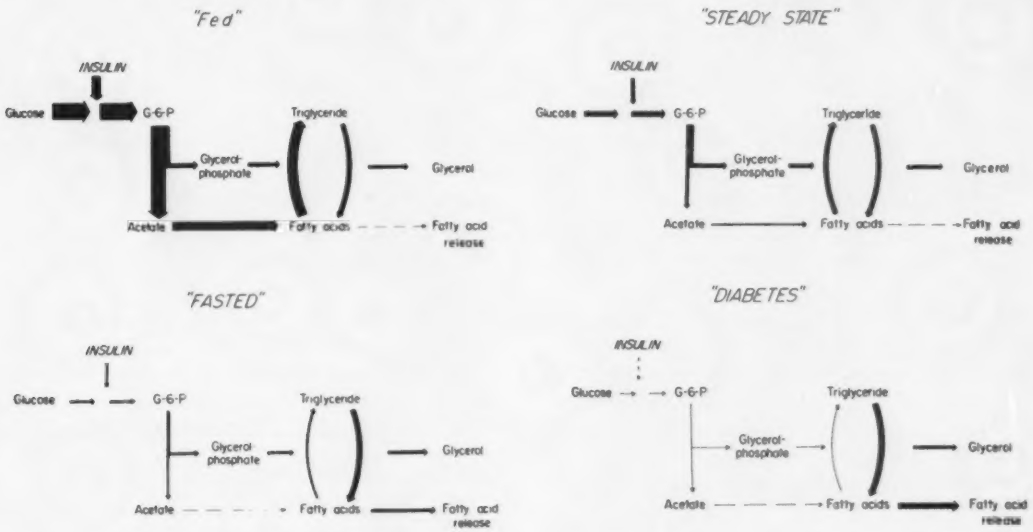


Fig. 2. Metabolism of glucose in adipose tissue. The thickness of the lines is representative of the number of carbons metabolized per unit time. It is obvious from the scheme that diabetes is merely an accentuation of the metabolic process of fasting, namely, enhanced free fatty acid release due to inability to form glycerol phosphate.

Free Fatty Acids

The next classical concept to be altered in the past few years is the previously accepted role of glucose as the body's most important source of energy. The work of Dole[27] and of Gordon,[28] recently reviewed by Fredrickson and Gordon[29] has stressed the role of circulating free fatty acids as probably the major circulating fuel. These free fatty acids, formerly called unesterified fatty acids (UFA's) or non-esterified fatty acids (NEFA's), are released by adipose tissue into the extracellular fluid and circulate tightly bound to plasma albumin. Certain tissues, for example, the heart, may utilize free fatty acids as its sole source of energy.[30-33] Indeed, it seems that only the nervous system, as represented by brain, necessarily requires glucose as an energy source. Since these free fatty acids originate from adipose tissue, the mechanism of their liberation, and particularly the factors which control this mechanism become extremely important in the understanding of homeostasis and the alterations in homeostasis as seen in the diabetic state.

enzymatic machinery for the activation of glycerol. In adipose tissue, however, free glycerol, once produced by lipolysis, may be metabolized to only a limited degree.[34,35] The glycerol used in the synthesis of triglyceride has been shown to be an activated form of glycerol, glycerol phosphate.[36] Since adipose tissue lacks this capacity to effectively convert free glycerol to glycerol phosphate, a source of glycerol phosphate is necessary to re-esterify the free fatty acids to triglycerides in order to prevent their accumulation and release.[25] This source is glucose. However, as mentioned earlier, due to the exquisite role played by insulin in permitting glucose metabolism in this tissue, the glucose supply is regulated by the concentration of effective insulin. Thus, lack of insulin, by limiting the ability of glucose to be metabolized to glycerol phosphate, limits the rate of fatty acid esterification to triglyceride and thereby permits free fatty acids to accumulate in the adipose cell with their eventual release into the circulation (Fig. 2).

On the other hand, as shown by Hausberger[15] and

by Renold[21,36] and his group, higher concentrations of insulin increase the metabolism of glucose beyond that amount needed to synthesize glycerol phosphate and the excess is in turn utilized for fatty acid synthesis. insulin signals the fat cell to release its fat as free fatty acids. This latter reaction also probably necessitates some sympathetic nervous activity in the adipose tissue in addition to the "permissive" effects of

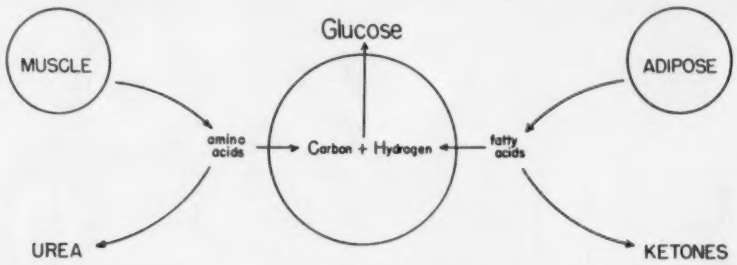


Fig. 3. Concomitant requirement of amino acid and fatty acid release from muscle and adipose tissue respectively in the process of gluconeogenesis by the liver.

Thus, modulations in the concentration of effective insulin signal the fat cell whether it should extract excess quantities of glucose from circulating fluids in the process of lipogenesis in order to expand its stored triglyceride pool. This relationship of adipose tissue and insulin places heretofore unestimated importance on the sensitivity of the β-cell to closely regulate the concentration of circulating effective insulin.

Numerous recent experiments from many laboratories have shown that factors other than lack of effective insulin may accelerate the release of free fatty acids from adipose tissue. For example, it has been shown for years that sympathetic denervation of fat followed by fasting results in a slower mobilization of fat in the denervated area compared to the inervated area.[37] Thus, the nervous system seems to play an important "tonic" role in fatty acid release,[38] probably by regulating the rate of lipolysis of triglyceride to free fatty acid and glycerol.[39] Likewise, epinephrine and nor-epinephrine[39-41] accelerate lipolysis, a logical alarm response analogous to the epinephrine effect on glycogenolysis in liver and muscle. In fact, such minor stresses such as discussion of emotionally charged topics are able to elevate free fatty acid concentrations in man.[42] In addition, thyroid,[43] growth,[44] adrenocorticotrophic[45] and other hormone preparations as well have been implicated in the release of free fatty acids from adipose tissue, but their physiological role in fat mobilization is as yet not clearly delineated.

Piecing the parts together, insulin signals the fat cell, as mentioned above, to expand its fat stores at the expense of blood glucose, and conversely, lack of thyroid, adrenocortical hormones and possibly other hormones as well. In the absence of effective insulin, free fatty acids are liberated from adipose tissue unopposed by esterification, and the concentration of free fatty acids in the plasma rises accordingly.

Muscle and Amino Acids

The preceding discussion would appear to favor adipose tissue as the primary target of insulin action. It is the opinion of the author that this is probably the case in respect to glucose and fat metabolism. On the other hand, the incorporation of amino acids into muscle protein has been shown to be exquisitely sensitive to insulin.[46,47] In an analogous manner to glucose in adipose tissue, insulin may serve to signal muscle to extract amino acids and to incorporate these amino acids into protein. Lack of insulin, therefore, would permit muscle to release its amino acid reserve, again analogous to the release of free fatty acids by adipose tissue when insulin is lacking.

A biochemist might have postulated the role of insulin in amino acid metabolism in muscle, since, if insulin is the "fed" hormone, lack of insulin or "fasting" places a gluconeogenic requirement on the liver to produce glucose for certain tissues, most notably the brain. The biochemist realizes that gluconeogenesis involves the reduction of two three-carbon acids (pyruvate) by hydrogen to form glucose. The hydrogens are readily derived from fatty acids with acetate as the "by-product." The three-carbon acid, however, cannot to any appreciable degree be derived from fat and must therefore arise from deamination of amino acid with urea as its "by-product." Gluconeogenesis, therefore, necessitates concomitant

utilization of fatty acids and amino acids with acetate (or ketone bodies, condensation products of acetate) and urea as respective waste "by-products." The biochemist would deduce that a signal (insulin, or more correctly, lack of insulin) must be transmitted to both adipose tissue and muscle as respective sources of fatty acids and amino acids—during fasting to render their stored products into the blood (Fig. 3).

The diabetic, whose insulin deficit surpasses that of the fasted normal, can be regarded as "superfasted." Amino acid release from muscle and fatty acid release from adipose tissue occur maximally when insulin is totally lacking, and these events are obviously reflected by loss of body fat and protein stores. Urea is probably benign, however, condensation products of accumulated acetate (that is, acetoacetate and β-hydroxybutyrate) are strong acids and when their concentrations rise beyond the renal threshold, they are excreted in the urine with sodium and potassium resulting in acidosis and eventually coma and death.

Conclusion

In summary, the concept of insulin action has evolved into a mechanism whereby the body alters its metabolism in favor of anabolic reactions, particularly fat synthesis. Decreased insulin action is a signal to the tissues to supply gluconeogenic precursors to the liver, thereby favoring overall catabolism. The concentration of effective insulin must thereby be exquisitely regulated, serving to effect the balance between the fed and fasting state, perhaps fluctuating several times daily in the normal meal-eating animal such as man. In the juvenile or ketotic diabetic, this signal is lacking and catabolism takes place, even in the presence of severe hyperglycemia.

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Follow-up on Aldosteronism

The man who described the first case of primary aldosteronism declared that after six years' observation he now believes the disease "will prove to be much more common than we think it is today."

Fifty-six cases of this "intriguing syndrome," which is completely curable by surgery, have been reported in the literature and 100 more are well documented, reported Dr. Jerome W. Conn of the University of Michigan Medical School, Ann Arbor.

In retrospect, he notes, it "was our good fortune to have encountered a most classical case of primary aldosteronism as the initial one." Very little has been added to the biochemical or symptomatological picture, although some "astute clinicians" have recognized cases in which classical manifestations have been missing.

In a situation, the diagnosis of which must lead to surgery, one desires "infallible diagnostic criteria," Dr. Conn added. Criteria have been worked out, but "experience in the past five years has taught us that if we insist on having all the classical findings we will diagnose only about 30 per cent of the cases." And early diagnosis is crucial.

Removal of the source of excess aldosterone production results in "dramatic disappearance of the entire syndrome in the vast majority of cases." The usual response is prompt re-arrangement of electrolyte and acid-base balances, usually completed by the third postoperative week. All the symptoms disappear abruptly.—Conference on Endocrine at Copenhagen—*World Medical News.*

An Integrated View of Glucagon

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GLUCAGON is one of the most interesting, powerful, and mysterious substances known to medicine. It has diverse physiologic functions; it is effective in minute doses, but we don't know just why it is in the human body.

In this review I would like to summarize briefly our biochemical and physiologic knowledge of this hormone and discuss its experimental and practical clinical uses. The interested reader is referred to several extensive reviews.[1-4]

Glucagon's life history is intimately connected with its neighbor, insulin. In fact, shortly after the discovery of insulin it was noted that before the blood sugar went down after insulin, it rose in the first few minutes. Kimball and Murlin[5] postulated a second substance (which they named glucagon) in the pancreatic extracts (Fig. 1). After insulin is inactivated with cysteine, the hyperglycemic effect can be shown.

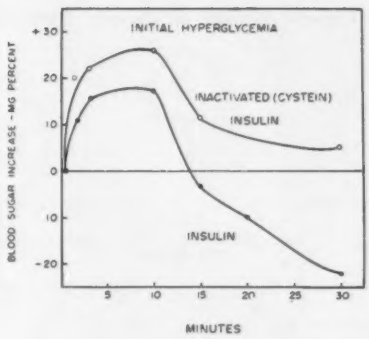

Fig. 1. Effect of active and cysteine-inactivated insulin on blood sugar. Note the initial hyperglycemia which is due to glucagon.

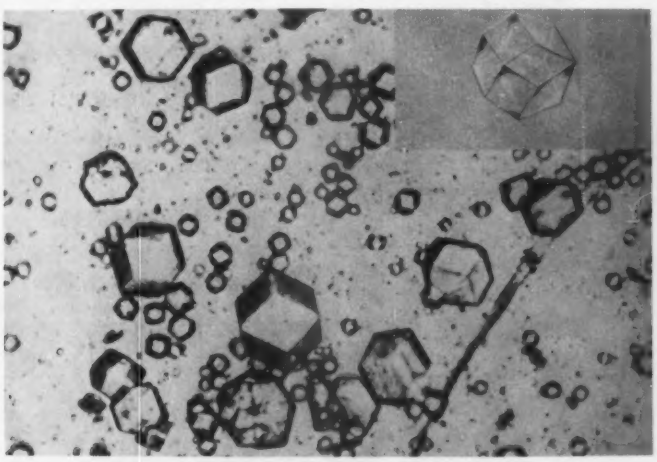

Fig. 2. Glucagon crystals (after Staub, Sinn, and Behrens[6]).

After thirty years of conflicting observations, the blurred picture finally cleared. There *is* a substance liberated by the alpha cells of the islets of Langerhans in the pancreas which goes to the liver. In 1953, Staub, Sinn, and Behrens,[6] in our laboratories, were able to prepare a crystalline material from pancreatic extracts which is hyperglycemic and glycogenolytic (Fig. 2).

Presented at a meeting of the Pan American Medical Association, Mexico City, May 5, 1960.

From the Medical Division, Lilly Research Laboratories, Indianapolis, Indiana.

Chemical Structure of Glucagon

Molecular weight - 3485

29 amino acids as a straight-chain polypeptide

Complete amino acid sequence known

--Bromer, Sinn, Staub, Behrens
J. Am. Chem. Soc. 78:3858, 1956

Fig. 3. Chemical structure of glucagon (after Bromer *et al*[2,7]).

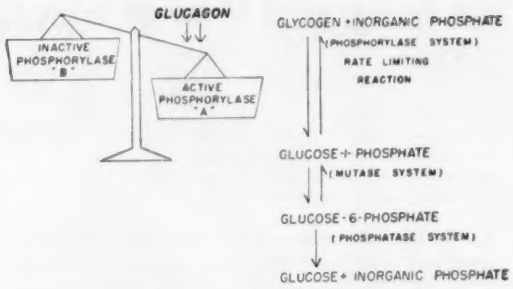

Fig. 4. Schematic representation of the function of glucagon (from Kirtley, Waife, Helmer, and Peck[10]).

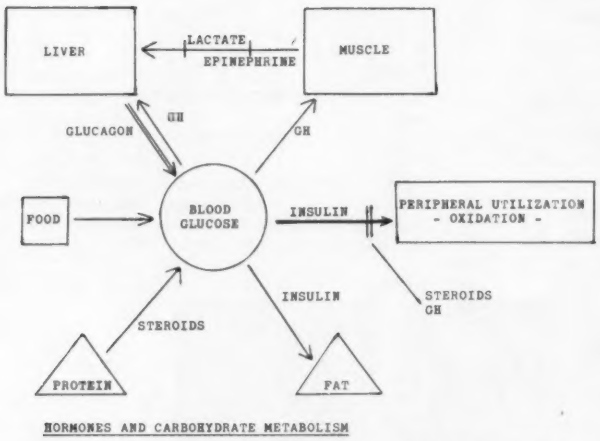

Fig. 5. Schema of hormonal actions on carbohydrate metabolism. Note the position of glucagon and insulin in this diagram.

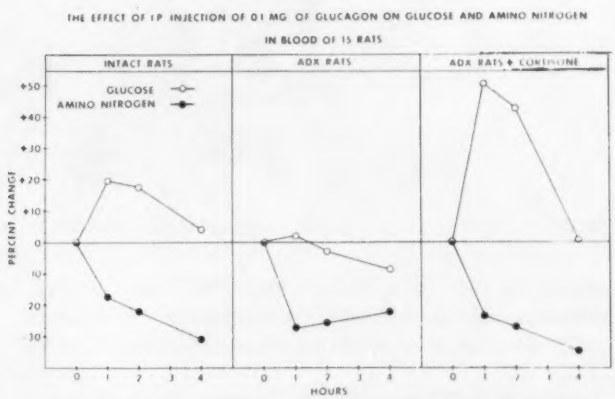

Fig. 6. Effect of glucagon on blood glucose and amino nitrogen (from Helmer *et al*[8]).

In 1956 our associates scored again by determining the chemical structure (Fig. 3).[2,7]

The functions of glucagon may be described as follows: It throws the balance in favor of active phosphorylase (in the liver only) which has the effect of breaking down liver glycogen to glucose (Fig. 4).

In a teleologic sense, glucagon may be said to have the task of making the liver's store of carbohydrate available to the body as a whole. The role of this and other hormones is shown in Figure 5.

In some respects, glucagon resembles epinephrine in action. Both are short-acting substances which raise blood sugar. However, epinephrine acts also on *muscle* glycogen and its action can be blocked by ergotamine, which is not true for glucagon. In some respects, glucagon resembles corticosteroids, especially in causing breakdown of protein (with some conversion into glucose, gluconeogenesis) and excretion of nitrogen products.

Figure 6 shows some data from Dr. Helmer, of our laboratory at the Marion County General Hospital.[8] You will note that the fall in blood amino acid after glucagon is not related to the rise in blood sugar. After glucagon there is an increase in urea (N) excretion as well as a fall in blood amino acid nitrogen.

Glucagon is, therefore, a catabolic agent, and one may *speculate* that the body begins to break down its protein—and fat—stores when liver glycogen is depleted via the metabolic signal offered by glucagon, which is probably secreted when the blood sugar falls to hypoglycemic levels. In other words, the liver becomes depleted of glycogen: blood sugar falls. This stimulates glucagon secretion: glucagon causes protein catabolism with new formation of carbohydrate from protein; the new carbohydrate keeps the "motor running"—for a time at least.

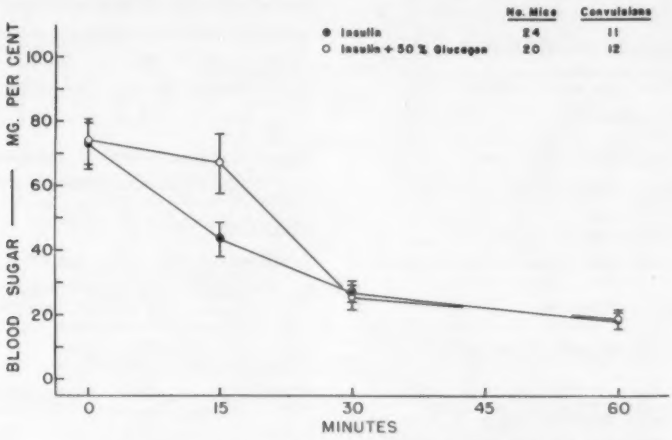

Fig. 7. Blood sugar response of mice to insulin and insulin plus glucagon. Note that the addition of 50 per cent glucagon did not affect the hypoglycemic action of Insulin (from Root, Ellis, and Staub[9]).

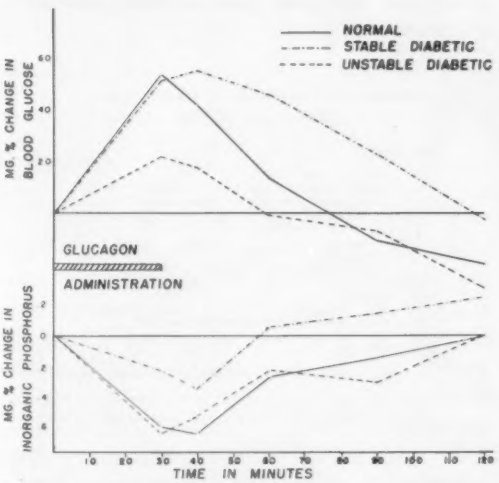

Fig. 8. Effect of glucagon on blood sugar and serum inorganic phosphate in "stable" and "unstable" diabetic subjects (from Kirtley, Waife, and Peck: Proc. Soc. Exper. Biol. & Med., 83:387, 1953.)

One of the many questions that arose several years ago when glucagon was actively studied was, does glucagon interfere with the action of insulin? If there is glucagon in an insulin preparation, would it interfere with the insulin assay? Dr. Mary Root and associates, of our group, studied this problem (Fig. 7).[9] Note that even with large amounts of glucagon pres-

ent, the insulin effect is not altered. Assay of our commercial insulin reveals a glucagon content of one-half of 1 per cent or less.

Our group[10] was interested in seeing whether stable

Metabolic Effects of Glucagon

1. Activation of liver phosphorylase
   → glycogenolysis → hyperglycemia
2. Catabolism of protein →
   → gluconeogenesis
   → increased nitrogen excretion
   → decreased blood amino acid
3. Inhibition of gastric motility and secretion
   → satiety (?)
4. Increased electrolyte excretion
5. Effect on fat metabolism → decreased formation of fatty acids
6. Increase in oxygen consumption

Fig. 9. Metabolic effects of glucagon.

and brittle (or juvenile) diabetics differ in their response to glucagon (Fig. 8). These early data show that there are indeed some differences in response to single doses of glucagon. Just how this fits into the pathogenesis of the two types of clinical diabetes is still speculative.

Glucagon for Termination of Insulin Coma

Advantages

1. vs. glucose
   --decreased volume and viscosity
   --no local reactions (thrombosis)
2. vs. tube feeding
   --faster
   --easier
   --decreased danger of aspiration
3. Safety
4. Decreased weight gain during IST

Disadvantages

Patient must eat shortly after awakening.

Fig. 10. Some current clinical uses of glucagon.

Glucagon also has an interesting effect on the gastrointestinal tract.[1] It produces a prompt decrease in motility and secretion. In very large doses, it can produce nausea. With the diminished gastric activity there is a suppression of the sensation of hunger. This has led to speculation that glucagon may be somehow involved in the satiety mechanism. Certainly, because of the interrelation of obesity and diabetes, this subject deserves further research.

Some of the metabolic functions are illustrated in Figure 9.

At present, there are two primary *clinical* uses of glucagon: treatment of insulin reactions among diabetics and termination of therapeutic insulin coma (Fig. 10).[11-17]

Small doses, only about 1 mg., of glucagon administered parenterally lead to arousal from hypoglycemic coma in about ten to fifteen minutes, the blood sugar rising about 50 mg. per 100 ml. The patient should then take carbohydrate by mouth to prevent relapse.

Clinical Uses of Glucagon

Diabetes

Insulin reactions due to
- overdosage
- inadequate food intake
- inability to utilize food
- strenuous exercise

Insulin Shock Therapy

Replaces glucose (intravenous or by gavage) in most cases

Fig. 11. Use of glucagon for termination of insulin coma.

Usually one dose is adequate. Of course, the physician has to use his own judgment in every case; if coma is very deep or prolonged, hypertonic glucose should be given. But for the diabetic patient at home, glucagon would seem to be very useful in emergencies, for it can be given by members of the family in a fashion similar to insulin. It also saves precious time and spares personnel when used to bring people out of insulin shock in the treatment of mental disease.

Other Uses under Study

1. Glycogen storage disease (von Gierke)
2. Islet-cell carcinoma of pancreas
3. Idiopathic hypoglycemia
4. Leucine-induced hypoglycemia
5. Anti-tumor effect (experimental)

Fig. 12. Other clinical states in which glucagon is being studied.

The advantages of a simple injection of glucagon are shown in Figure 11. The material may be given subcutaneously, intramuscularly, or intravenously. The only differences are in the speed of the effect.

Several other conditions associated with hypoglycemia are currently under study (Fig. 12).

Johnson and Wright,[18] in our laboratories, reported

last year that glucagon in large doses had a carcinostatic effect on a variety of experimental rat tumors. There is *no* clinical application to this finding, and I mention it only to prove my point that glucagon is a most interesting and mysterious substance.

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New Uses For Aspirin

Small daily doses of aspirin can lower blood cholesterol, relieve the symptoms of diabetes, and can act like thyroid where there is insufficient metabolic activity. Salicylic acid preparations have been used since antiquity as a remedy for rheumatic pains. Now, according to Chauncey D. Leake, M.D., in *The New Physician*, July, 1960, aspirin has been found to stimulate the hormone system of the body creating an increased flow of the hormones so necessary for healthy activity. He wrote:

"The safety of aspirin is such as to make it readily available without prescription everywhere—and it is not expensive anywhere. Since the drug leaves the body in four to six hours, its dosage must be repeated that often in order to maintain effectiveness.

"The therapeutic application of the actions of aspirin to diabetes mellitus is startling. It reduces blood sugar and glycosuria, controls ketosis, improves glucose tolerance, and well supplements the action of insulin. It has already been useful in controlling diabetics who do not wish insulin injections. Its simultaneous reduction of hypercholesteremia may prove to be especially beneficial in a disease in which premature vascular degeneration is so common.

"During the past six decades, under the common name, aspirin, it has become the most used drug, world over, for relief of congestive pain and for removing the symptoms of fever. Its remarkable safety has contributed to this success, in spite of its tendency (about 5 per cent) to cause allergic reactions."

Insulin Resistance

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THE INSULIN requirement in the human following total pancreatectomy is said to be approximately 40 units of insulin per day. Since many patients with spontaneous diabetes appear to have insulin requirements in excess of this amount, absolute insulin deficiency does not appear to be an adequate explanation for their large insulin requirements. In this respect, diabetes is quite different from Addison's disease and hypothyroidism where hydrocortisone and thyroid requirements respectively do not show such great variability from patient to patient. In addition to the marked variation of insulin requirements among diabetic patients, there are a small group of patients who, in the absence of acidosis, infection or endocrine disturbance, require over 200 units of insulin per day and have been arbitrarily defined as having chronic insulin resistance. Temporary resistance to insulin is frequently seen associated with diabetic acidosis, infections and endocrine disturbances such as Cushing's syndrome and acromegaly. This paper presents the results of some of our studies demonstrating substances in the plasma which might provide an explanation for the resistance to insulin in the clinical situations just mentioned.

The technique used in these studies is based on the ability of insulin to stimulate glucose uptake and glycogen deposition by rat hemidiaphragm. In these experiments one hemidiaphragm is exposed to test plasma, buffer and insulin while the control hemidiaphragm from the same animal is dipped in plasma and buffer without insulin. Subsequently, the diaphragms are washed in buffer and then incubated in buffer and glucose for ninety minutes. At the end of the incubation period, the glucose disappearing from the medium or the glycogen content of the diaphragms is determined. In the presence of normal plasma, the hemidiaphragm exposed to insulin will deposit more glycogen and take up more glucose than its control. This increment due to insulin is referred to as the insulin effect. The abolition of this effect by the test plasma is interpreted as evidence for the presence of an insulin antagonist in the test plasma.

Insulin antagonists have been implicated in the etiology of chronic insulin resistance. Over twenty years ago, Banting demonstrated that the plasma of such a patient contained something which protected the fasted rabbit from hypoglycemia. Since that time, there have been numerous case reports concerning diabetic patients with chronic insulin resistance whose plasma contained an insulin antagonist, most likely an antibody to insulin. Berson has very thoroughly discussed the studies which he and his colleagues have done on this antibody to insulin. He has shown that the insulin-binding capacity of plasma from patients with chronic insulin resistance is much greater than that found in the non-insulin resistant patient. His detailed studies concerning the kinetics of the reaction between insulin and the insulin antibody promise to provide a better understanding of the role of this substance in clinical diabetes. In patients with chronic insulin resistance it has been possible to demonstrate an antagonist in the plasma which might account for the resistance. Table I shows that in the presence of normal plasma, the rat hemidiaphragm exposed to insulin will take up 2.74 mg. of glucose per gram of muscle more than the control hemidiaphragm not exposed to insulin. This difference, referred to as the insulin effect, is not significantly altered by using dilutions of plasma up to 1:1000. Table II records the results obtained using plasma from some patients with chronic insulin resistance, indicating the presence of an insulin antagonist. Note the marked decrease in the insulin effect as com-

TABLE I. INSULIN EFFECT IN THE PRESENCE OF NORMAL PLASMA

Dilution of Plasma	Mg. Glucose/Gm. Muscle	Number of Experiments
Undiluted	2.74±0.17	51
1:10	2.41±0.10	89
1:100	2.07±0.23	15
1:1000	2.16±0.27	3

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pared with the normal (Table I). Immunologic studies indicated the antibody nature of this antagonist. There was a poor correlation between the titer of the antagonist and the daily insulin requirement.

TABLE II. OTHER PATIENTS WITH CHRONIC INSULIN RESISTANCE

Patient	Insulin Dosage	Dilution of Plasma	Insulin Effect
Ov	400	Undiluted	0.20±0.46 (6)
Bu	256	Undiluted	0.50±0.77 (3)
Fr	220	Undiluted	0.08±0.21 (3)
Th	250	1:10	0.50±0.28 (3)
Ch	700	1:10	1.00±0.75 (3)
St	580	1:10	0.19±0.15 (3)

Adrenal steroids have been used with some success in the treatment of chronic insulin resistance. Table III summarizes the findings in a case successfully treated with prednisone. Before prednisone the daily insulin requirement of this patient was 1800 units, and insulin antagonist was demonstrable even when his plasma was diluted 1:100. Only when the plasma was diluted 1:1000 was it possible to recover the effect of the added 0.01 units of insulin. Following successful prednisone therapy, his daily insulin requirement fell to 80 units and, although an antagonist to

TABLE III. PATIENT WITH CHRONIC INSULIN RESISTANCE TREATED WITH PREDNISONE

Dilution of Plasma	Insulin Effect	
	Pre-Prednisone	Post-Prednisone
Undiluted		0.72±0.67 (3)
1:10	0.85±0.36 (3)	3.26±0.32 (3)
1:100	0.33±0.40 (3)	
1:1000	2.78±0.62 (3)	

insulin was still present, it was decreased in amount. The mechanism of action of steroids in such cases remains to be elucidated. In another case that was successfully treated with steroids, the rate of insulin-I^{131} disappearance from the plasma before and after steroid therapy was studied. Successful steroid therapy in this case did not accelerate the rate at which insulin-I^{131} left the plasma.

It has also been suggested that the augmented amounts of antibody found in patients with chronic insulin resistance are not the cause of the insulin resistance but only a manifestation of repeated injections of large amounts of insulin, necessary for the control of the diabetes. Clinically it has occasionally been observed that diabetics with chronic insulin resistance and circulating insulin antagonist do as well on diet and no insulin as they do when given large doses of insulin. An explanation for this hypothesis proposes that the insulin antibody was antagonistic to commercial insulin only and not to the endogenous insulin of the patient. These patients presumably had sufficient endogenous insulin to avoid ketosis, provided that observance of a prescribed diet was rigid. However, the correctness of this explanation is open to question since we and others have shown that the insulin antagonist present in patients with chronic insulin resistance does indeed inhibit the effect of human insulin (Table IV). We must look to future studies to further clarify the place of insulin antibodies in the etiology of chronic insulin resistance.

TABLE IV. ABILITY OF HUMORAL INSULIN ANTAGONIST FROM PATIENT WITH CHRONIC INSULIN RESISTANCE TO INHIBIT THE EFFECT OF HUMAN INSULIN

Serum	Type of Insulin	Insulin Effect
		Micromoles Glycogen (Glucose Equivalent) Per Gram of Tissue Mean ± S.E.M.
J.C. 12-19-56	Beef-Pork 0.2 unit	0.58±0.66 (3)*
J.C. 12-19-56	Human 0.2 unit	1.75±0.95 (3)
Normal	Human 0.2 unit	6.48±0.06 (3)

( )*Number of determinations.

In addition to insulin antibodies, other plasma insulin antagonists, clearly not antibodies, have been demonstrated in certain other diabetic situations. Table V shows the results obtained using plasma from some untreated patients with newly-discovered diabetes. Although glycosuria and ketonuria were present in all patients, diabetic acidosis was absent. Plasma from the first two patients was capable of inhibiting the

TABLE V. NEW DIABETICS REQUIRING INSULIN

Patient	Dilution of Plasma	Insulin Effect	
		Before Insulin	After Insulin
Wh	Undiluted	0.32±0.30 (3)	2.49±0.61 (6)
Ke	Undiluted	1.16±0.22 (3)	2.49±0.44 (3)
Sh	Undiluted	2.36±0.12 (3)	
Or	Undiluted	2.27±0.38 (3)	

effect of insulin, while there was no evidence of insulin inhibition in the last two cases. Clinically, there were no distinguishing features between the two patients with and the two patients without an insulin antagonist. Plasma was obtained again from the first two cases several days after insulin therapy had been instituted, and at that time, the diabetes had been controlled. No insulin antagonist was demonstrable. The

evanescent nature of the antagonist in this situation is reminiscent of that found during diabetic acidosis.

Infections in the patient with diabetes are frequently associated with an increase in insulin requirement and with some degree of insulin resistance. Table VI summarizes the results obtained using plasma from

TABLE VI. DIABETICS WITH INFECTIONS

Patient	Dilution of Plasma	Insulin Effect
Wo	1:10	1.04±0.47 (3)
St	Undiluted	1.11±0.32 (6)
Os	Undiluted	1.56±0.37 (3)
Ha	Undiluted	2.08±0.39 (6)

diabetic patients with infections. Patient WO had an acute staphylococcal abscess and his plasma, diluted 1:10, inhibited the effect of 0.01 units of insulin. The diabetes of patient ST was out of control as a result of infectious mononucleosis. His plasma also exhibited an insulin antagonist. Patient OS entered the hospital with acute appendicitis. Although the insulin effect was lower than in any of the experiments with normal plasma, significant insulin antagonism was not demonstrable. The final patient (HA) with an acute pyelonephritis due to Escherichia coli did not have any insulin antagonist in her plasma. Unfortunately, it was not possible to test plasma from these patients after the infections had been resolved in order to determine if any insulin antagonist was still present. The antagonist present in patient WO during infection had some characteristics similar to the antagonist present in a patient with diabetic acidosis, but different from that found in the patient with chronic insulin resistance.

The procedure used in these experiments was modified somewhat so that the insulin-stimulated hemidiaphragm was exposed to the plasma first, then washed in buffer and dipped in insulin before being incubated in glucose. In this way the plasma, insulin and diaphragm are not in contact simultaneously. It has been demonstrated previously that the insulin antagonist present during diabetic acidosis was still active under these circumstances, while the antagonist present in the patient with chronic insulin resistance would no longer inhibit the effect of insulin. In the case of chronic insulin resistance, plasma, insulin and diaphragm must all be together in order to inhibit the effect of insulin. The inhibitory effect of plasma is lost when the diaphragm is pre-treated with plasma. In contrast, the antagonist present in patient WO during his infection was still capable of inhibiting insulin even though the plasma, insulin and diaphragm were not present simultaneously. In this respect the insulin antagonist during an infection in this diabetic resembles that present in the patient with diabetic acidosis. When normal plasma is used, this change in procedure does not modify the insulin effect. Many cases of diabetic acidosis are precipitated by infection; hence it would seem reasonable for the insulin antagonist present in some diabetics during infections to be similar to (or possibly identical with) the antagonist found in patients with diabetic acidosis.

It is possible to find evidence of an insulin antagonist in some, but not all, cases of diabetic acidosis. In these studies glycogen deposition by rat diaphragm was measured instead of glucose uptake. The insulin effect in the presence of normal plasma is 5.35 micromols of glycogen per gram of muscle. In the cases

TABLE VII. ACTIVITY OF VARIOUS PROTEIN FRACTIONS OF INSULIN ANTAGONIST SERUM

Fraction	Equivalent Amount of Whole Serum	Insulin Effect: Micromoles (Glucose Equivalent) Per Gram of Tissue Mean ± S.E.M.
Albumin	0.15	7.23±0.74 (3)*
α_1 Globulin	0.15	1.41±0.99 (3)
α_2 Globulin	0.15	4.72±2.26 (3)
β Globulin	0.15	8.52±1.77 (2)
γ Globulin	0.15	8.17±2.64 (3)

( )*Number of determinations.

where an antagonist was present during diabetic acidosis, it was not present several days later after the acidosis had been successfully treated. Although previously, both decreased plasma pH and increased adrenal corticoid activity had been suggested as the cause of this temporary insulin resistance, it was not possible to demonstrate any antagonist in sera obtained from some patients with uremia whose plasma pH and CO_2 combining power were just as depressed as those in patients with diabetic acidosis. The addition of large amounts of hydrocortisone to normal plasma did not produce insulin antagonism. Some patients had no circulating insulin antagonist, yet had very high levels of plasma hydrocortisone. Other studies have suggested that this antagonist is not glucagon and possessed no insulinase activity. It did not appear to interfere with the binding of insulin to muscle. By starch block electrophoresis of plasma proteins, the antagonist activity in diabetic acidosis is shown to reside primarily in the alpha-1 globulin fraction (Table VII). This is in contrast to the gamma-globulin or interbeta-gamma globulin location of the insulin antibody present in patients with chronic insulin

resistance. The antagonist present during diabetic acidosis is still capable of inhibiting the effect of insulin when insulin and plasma are exposed to the rat diaphragm separately.

An insulin antagonist is present in some cases of acromegaly associated with diabetes. Clinically it has been observed that the diabetes present in acromegalics is often characterized by a degree of insulin insensitivity. In experimental animals the diabetes resulting from repeated injections of growth hormone is also refractory to insulin. Table VIII records the presence of this antagonist in some patients with acromegaly. As yet, this antagonist has not been characterized.

TABLE VIII. DIABETICS WITH ACROMEGALY

Patient	Dilution of Plasma	Insulin Effect
Ma	Undiluted	0.97±0.73 (3)
St	Undiluted	1.20±0.25 (6)
Ja	Undiluted	−0.30±0.35 (3)
Wy	Undiluted	2.28±0.23 (3)

Summary

Circulating inhibitors of insulin have been demonstrated in several clinical situations in the diabetic. In chronic insulin resistance the antagonist is probably an antibody to insulin and its effective titer can often be reduced by steroid therapy. The mechanism of the steroid effect is unknown. This antibody appears to be different from the antagonist present during some cases of diabetic acidosis and infections in the diabetic. Whether the antagonist in the latter two instances is identical is not known. In some new diabetics an antagonist to insulin can also be demonstrated. Its presence is transient. The exact nature of this antagonist is unknown also. Its etiologic role in the production of diabetes is still unanswered. It is also possible that the insulin resistance observed in the acromegalic patient with diabetes is due to an insulin inhibitor.

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Pathology of Lung Diseases

An improved method for studying the pathology of lung diseases has been developed by joint studies of Hollis G. Boren, M.D., and Bernard J. Blumenthal, M.D., of the Houston, Texas, Veterans Administration hospital and Baylor University College of Medicine, and William Hentel, M.D., and A. N. Longfield, M.D., of the Albuquerque, N. Mex., VA hospital.

Allowing for study of lung tissue in three dimensions, it offers a new approach to the unknown problems of pulmonary anatomy and pathology. At present, the research team is concerned with a number of lung diseases, especially emphysema and bronchitis.

"Three-dimensional study of the lung will allow investigators to become familiar with the actual architectural pattern that has been relatively unknown to those who have studied lung anatomy and pathology by conventional methods," Dr. Boren said.

Key to the new method is fixing the lung specimen in an inflated state more closely approximating the natural state. A formaldehyde vapor is passed through the lung for five days during the time fixing occurs. To prevent deflation and shrinkage of the lung, as well as to allow complete drying, air alone then is passed through the lung for an additional seven days.

The specimens obtained are dry, rigid, non-fragile, and inflated to a size closely approximating the living state. They may be studied almost in their entirety by cutting sections which can be viewed by stereoscopic microscopy or more conventional means.

Differential Diagnosis of Hyperglycemia and Melituria

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NOT LONG AGO, I was told that diabetes is a hobby, not a disease. This is a pleasant idea and one to warm our hearts. Unfortunately, it is highly unrealistic. To tell a patient he has diabetes is to deal a stunning blow to his emotional composure, and labeling him a diabetic jeopardizes his financial future. Consequently, to diagnose a trivial deviation of carbohydrate metabolism as diabetes mellitus is more than a trivial error. Perhaps equally or more serious is the error of failing to recognize the case of impaired glucose tolerance whose cause, though it may seriously threaten the patient's life, is correctable or controllable.

Definition

The subject before us is notorious for presenting difficult questions of definition. Without devoting all of the allotted space to semantic arguments, I feel compelled to deal with some of these. The first is the definition of diabetes mellitus. I know of none that is universally accepted. For the purposes of this discussion, diabetes mellitus will be defined as a disease of unknown cause characterized by permanent impairment of glucose tolerance. A virtue of this definition is that it makes possible separation of those cases of impaired glucose tolerance with recognizable cause and those of normoglycemic melituria from the vast mass of what must still be called "true" diabetes.

But the definition has several defects. Only two of these will be mentioned. One is that it defines the disease entirely in terms of one aspect of carbohydrate metabolism. Another, and the one I would like to examine, is that the phrase, impaired glucose tolerance, itself has an imprecise meaning.

At first thought it would seem unnecessary to devote space to defining "glucose." Yet, in many laboratories "blood glucose," as it is determined and reported, is only partly glucose. Many popular techniques measure in one lump, so to speak, a number of other reducing substances, such as glutathione, cysteine, and ergothioneine which, as far as I know, have little or no significance in the diagnosis of diabetes. It was thought that the nonglucose reducing substances contributed a fairly constant component (20 to 30 mg. per 100 ml.) to the value obtained for blood glucose concentrations by these techniques and were therefore relatively unimportant in the detection of hyperglycemia. Mosenthal and Barry[1] showed that this is not correct. Schales and I[2,3] have confirmed their observation using another method of determination. In examination of 332 samples of blood, we noted that the differences between the value for total reducing substances and those for glucose were not 20 to 30 mg. per 100 ml. but 6 to 75 mg. per 100 ml. In a number of instances blood that contained a normal concentration of glucose seemed to be hyperglycemic because of a large concentration of nonglucose reducing material.

TABLE I. SOME NON-DIABETIC CAUSES OF IMPAIRMENT OF GLUCOSE TOLERANCE

A.	Diet—carbohydrate starvation
B.	Exogenous hormones
	1. ACTH and some adrenal cortical hormones
	2. Insulin
C.	Prolonged immobilization
D.	Nonspecific "stress," e.g. burns, acute and chronic infections, operations
E.	Obesity
F.	Hepatic insufficiency
G.	Glycogen storage disease
H.	Certain pancreatic lesions
	1. Carcinoma of the pancreas
	2. Acute pancreatitis and sequelae
	3. Post-pancreatectomy state
	4. Islet cell tumors
I.	Hemochromatosis
J.	Postgastrectomy state
K.	Uremia
L.	Certain endocrinopathies
	1. Acromegaly
	2. Cushing's syndrome
	3. Pheochromocytoma
M.	Certain brain injuries

Finally, in our semantic progress, we come to the phrase "impairment of glucose tolerance." Most people would agree that consistent, substantial elevation of fasting blood sugar concentration is adequate evidence of impaired glucose tolerance. In the absence of this, some definition of normality, and by inference abnormality, of the response to a glucose load test must be sought. Of these tests the most commonly used is the simple oral glucose tolerance test. With respect to interpretation of this test, the American Diabetes Association suggested the following as normal: a fasting value below 100 mg. per 100 ml., the two-hour value

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falling to at least this level, and a value not in excess of 150 mg. per 100 ml. at any time during the procedure. All these values are for venous blood using a "true" glucose method. But other definitions are sometimes used. For example, Conn[4] considered a value of 160 mg./100 ml. at one hour and 110 mg./100 ml. at two hours to be normal.

In recent years, evidence has been presented that in this test minor deviations from normalcy, according to the standard definition, lack precise clinical significance. For example, in a prognostic study Ungar and Madison[5] observed that, after five to seven years, among forty-six people who originally showed minor abnormalities during the test, only 15 per cent had become overtly diabetic. More precise tests of the rate of

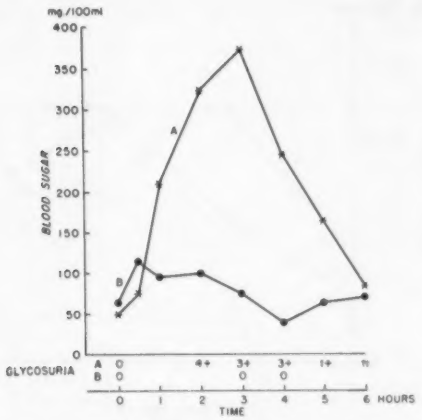

Fig. 1. Patient's glucose tolerance curves after a three day fast (A) and after three days of normal eating (B).

glucose removal from the blood have been developed but in these, too, the limits of normal variability appear to be in doubt. It becomes evident, therefore, that we are not quite sure where normal glucose tolerance ends and impairment begins. This uncertainty must be kept in mind when one is considering making the diagnosis of diabetes in doubtful cases on the basis of the glucose tolerance test alone.

Non-diabetic Causes of Impaired Glucose Tolerance

In Table I are some *nondiabetic causes of impaired glucose tolerance.* If for nothing else, the table is notable for its length. Each of the items should be considered, however briefly, in the differential diagnosis of diabetes mellitus. I would like to give examples of a few of them.

The effect of starvation on glucose tolerance is shown dramatically in Figure 1. The first highly abnormal result of an oral glucose tolerance test, associated with glycosuria, was found after the patient had

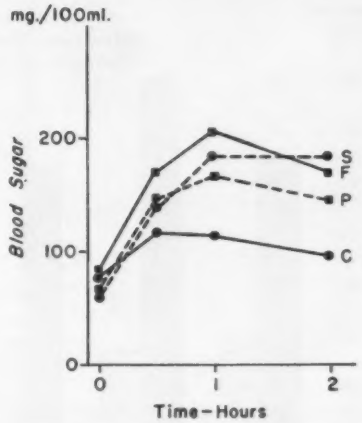

Fig. 2. Composite curves showing the effect of diet on the glucose tolerance of four groups of normal young adults. The groups were fed nothing but carbohydrate (C), protein (P), fat (F), or water (S), respectively, for two days before the glucose tolerance tests. (From Locke, William: Diagnosis of non-diabetic hyperglycemia and melituria. J. Louisiana State M. Soc., 107:433, 1955. After Sweeney.[6])

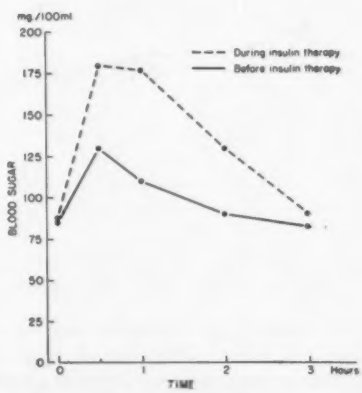

Fig. 3. Effect of insulin therapy on the glucose tolerance of non-diabetic people (after Appel and Hughes.[7])

fasted for three days. The second test was done later, after three days of normal eating and the result was normal. The important dietary deficit responsible for abnormalities of this kind is carbohydrate, as Figure 2,

prepared from Sweeney's data,[6] shows. Four groups of normal young adults were starved, fed fat alone, protein alone and carbohydrate alone, respectively. After two days, glucose tolerance was normal in the group fed carbohydrate but not in any of the others.

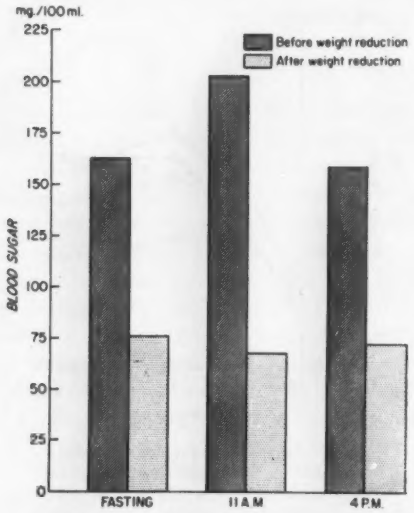

Fig. 4. Effect of diet, which led to a 13 per cent reduction in body weight, on a patient's blood sugar concentration.

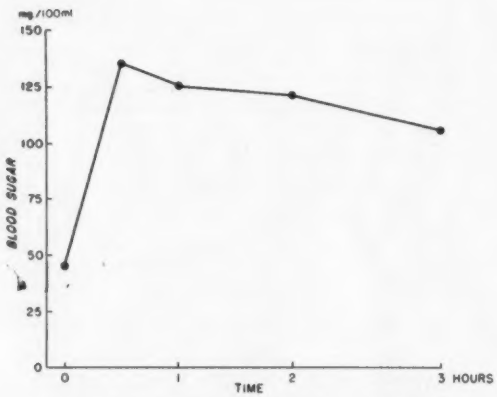

Fig. 5. Glucose tolerance curve in a case of glycogen storage disease.

The data of Appel and Hughes,[7] represented in Figure 3, suggest the hazards connected with attempting to diagnose diabetes in patients who have recently received insulin. In such circumstances, the results of the glucose tolerance test may be misleading.

In Figure 4 can be seen the effect of a 13 per cent reduction in body weight on a dieting patient's hyperglycemia. The blood sugar concentrations declined to less than half their previous levels.

Listed in the table are also some truly pathologic causes of impaired glucose tolerance. One of these is diffuse hepatic disease. Leevy and associates[8] reported their observations on ten alcoholic patients with hepatic disease who were hyperglycemic. Nine were glycosuric. Treatment of the hepatic disease was accompanied by improvement in carbohydrate tolerance in all. The most striking case was a patient whose fasting blood sugar was reduced from 460 mg. per 100 ml. to 90 and whose urinary excretion of sugar was reduced from 24 gm. per twenty-four hours to none. None of the patients knew of a diabetic relative.

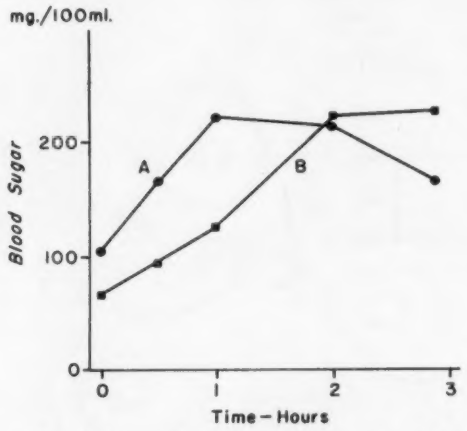

Fig. 6. Preoperative glucose tolerance curves of two patients (A, B) having islet cell tumors (Locke, William, *loc. cit.*).

A rather rare hepatic cause for impaired glucose tolerance is glycogen storage disease, as exemplified in Figure 5. The fasting blood sugar is low but the values at the second and third hours are abnormally high.

Parodoxically, functioning tumors of the islet cells are sometimes associated with glucose tolerance curves suggestive of mild diabetes. Whipple and Baumann[9] reported glucose tolerance studies in seventeen patients having islet cell tumors. Preoperatively, eight had glucose tolerance curves that have some resemblance to diabetic curves. In Figure 6 may be seen the preoperative glucose tolerance curves of two patients of mine. One curve is indistinguishable from those seen in mild diabetes; the other had the singular configuration of beginning at a low level and rising progressively during

the three hours of the test. This configuration is highly suggestive of the diagnosis of islet cell tumor.

The occurrence and degree of hyperglycemia among uremic patients are illustrated in Figure 7.

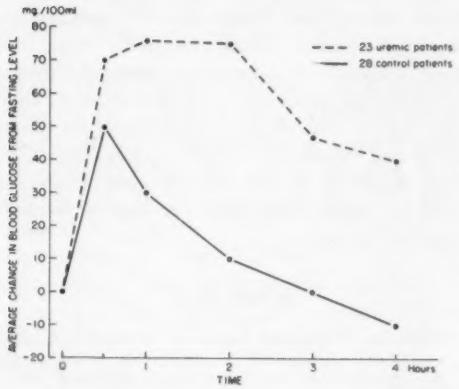

Fig. 7. Composite expressions of glucose tolerance of normal and uremic subjects.

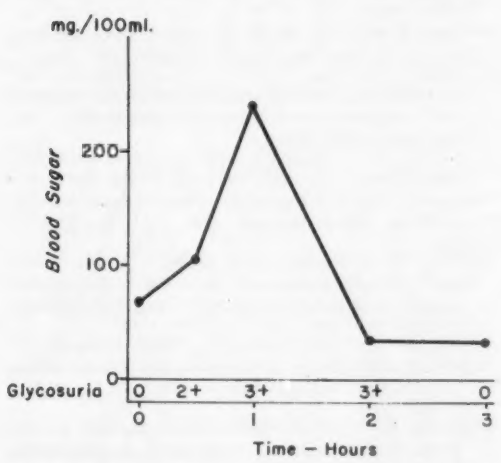

Fig. 8. Glucose tolerance curve of a patient who had had partial gastrectomy (from Locke, William, *loc. cit.*).

Figure 8 is from a post-gastrectomy case. The diagnosis of diabetes mellitus had been made on this patient before the true condition was recognized. Muir[11] found glucose tolerance curves with this configuration in thirty-four of eighty-eight post-gastrectomy patients. Glycosuria occurred during the test in each of the thirty-four.

Figure 9 illustrates that grossly abnormal glucose tolerance curves, sometimes seen in patients having pheochromocytomas, can be restored to normal by removal of the tumors.

Normoglycemic Melituria

Normoglycemic melituria is a much smaller clinical problem than the one just discussed. In Table II are listed some varieties of this condition. Normoglycemic

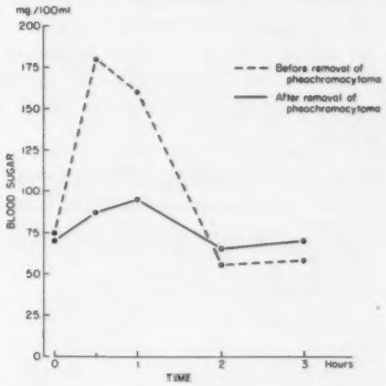

Fig. 9. Glucose tolerance curves of a patient before and after removal of a pheochromocytoma.

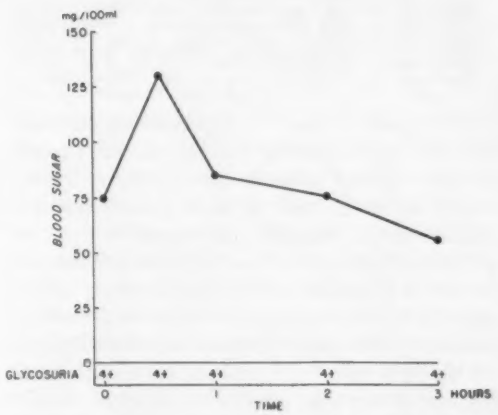

Fig. 10. Renal glycosuria in a man with a diagnosis of diabetes mellitus (from Locke, William, *loc. cit.*).

melituria is recognized by the finding of reducing substance in the urine, by an ordinary clinical laboratory reducing test, in association with normoglycemia. A few words of qualification may be in order. The galactosuria of galactosemia is associated with a high blood level of galactose and consequently of reducing material. The blood glucose level tends to be low but this may not be recognized unless a test specific for glucose is used. Sucrose gives a positive reaction to Benedict's test or the Clinitest procedure only after

hydrolysis. If the urine is tested by a glucose oxidase method, most of these conditions will remain undetected.

Figure 10 represents a glucose tolerance test in a case of renal glycosuria. Every urine test gave a 4+ reaction for sugar. The unfortunate patient, who came to us with the diagnosis of renal glycosuria, related that he had seen a score of physicians because of glycosuria and had been kept miserable by insulin induced hypoglycemic attacks before the correct diagnosis was made.

TABLE II. SOME CAUSES OF NORMOGLYCEMIC MELITURIA*

A. Renal glycosuria
   1. As an isolated finding
   2. During treatment with certain adrenal cortical hormones or ACTH
   3. During later months of pregnancy
   4. As part of Fanconi's syndrome
B. Melituria due to excretion of carbohydrates other than glucose
   1. Lactose
   2. Galactose
   3. Maltose
   4. Mannoheptalose
   5. Pentoses
   6. Fructose
   7. Sucrose**
C. Melituria due to excretion of substances other than carbohydrates
   1. Drugs: salicylates, camphor, menthol, chloral hydrate, morphine, pyramidon
   2. Alkaptone (homogentisic acid)
      a. As an isolated finding
      b. As a manifestation of ochronosis

*The term "melituria", as here used, signifies the presence in urine of substances which give a positive reaction to Benedict's test or to the Clinitest procedure.

**Sucrose gives a positive reaction to Benedict's test or to the Clinitest procedure only after hydrolysis.

(Reprinted from J. Louisiana State M. Soc., 107:433, 1955).

In conclusion, it may be suggested that we sometimes fall into the habit of thinking that the diagnosis of diabetes mellitus is simpler than it really is. Separation of the patient with impaired glucose tolerance from the person without it may depend as much on one's definition of normal as on any difference between the two of prognostic significance. Discovery of unequivocal impairment of glucose tolerance demands a painstaking initial examination and sometimes observation during a period of several months to exclude, or find, one of the many nondiabetic causes of this abnormality. These examinations are especially important if there is no family history of diabetes or if the fasting blood sugar concentration is normal. Anything unusual in the clinical manifestations of the disease requires renewed diagnostic efforts. Great caution should be exercised in diagnosing diabetes among acutely ill patients or those who have recently been injured. Glucose tolerance may return to normal upon restoration of normal health. Ideally, before the critical tests for the diagnosis of diabetes are made, the patient should have all significant correctable disorders eliminated and be well fed, active and free of the effects of drugs and exogenously administered hormones. The finding of glucose or other reducing substances in the urine is not sufficient evidence for making the diagnosis of diabetes mellitus.

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Bone Resistance to Acceleration

An anatomist at The University of Michigan Medical Center and engineers from Wayne State University are trying to find out how much acceleration a human can withstand before his bones start to break.

F. Gaynor Evans, Ph.D., at the U-M and Lawrence M. Patrick and Herbert R. Lissner of WSU are examining the effects of strenuous "G" forces on the intact human skeleton.

Their experiments are expected to help astronauts withstand the physical buffeting of re-entry into the earth's atmosphere, and promote safety for pilots being ejected from high-speed jet planes.

Most previous acceleration studies have been concerned with effects on blood circulation, nervous system and general human behavior.

Ocular Manifestations of Diabetes

Lorand V. Johnson, M.D.
Cleveland, Ohio

I HAVE THOUGHT of considering this a centennial address, since in 1859 there appeared in Germany two ophthalmic atlases, illustrating fundus changes visible by virtue of the ophthalmoscope described eight years previously by Helmholz, and which permitted a fairly accurate view of the fundus oculi.

The descriptions of the condition now called diabetic retinopathy were amazingly accurate, especially as relates to the well developed or advanced pathology. Physicians familiar with the appearance of diabetic retinopathy have no difficulty, in recognizing most of the visible changes seen today, by examining the plates on this condition contained in these early atlases.

As late as 1937, when I completed my ophthalmic residency, there was the belief that these hemorrhagic and proliferative changes, which were so destructive of vision, were associated with exceedingly mild diabetes, since the incidence of this form of failing vision was so frequently seen with these patients. The exceedingly great interest in the laboratory detection of diabetes had, by 1937, allowed a great number of patients to have been diagnosed for several years, and considerable ophthalmic speculation prevailed as to why diabetic retinal blindness was so seldom seen in the more severe cases of diabetes. Little consideration had been given to the possibility that the onset of diabetic hemorrhages and proliferative changes might not be associated with severity of the diabetes, or that these changes might be related to the duration in years that the individual had suffered the recently detected mild diabetes.

In perhaps the most extensive clinical statistical study, reported by Waite and Beetham in the New England Medical Journal, the eyes of 2,002 diabetics were compared to the eyes of 457 normal individuals.

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As will be discussed later, the results of this study showed conclusively that the onset of retinal hemorrhages and proliferative changes was related to the duration of disease and not to the severity of the disease or the degree of control. The problem of "why retinopathy was so seldom seen in the severe cases" was answered by the speculation that the more severe diabetics simply had not lived sufficiently long, during these early years of control, to develop blinding retinal hemorrhages and proliferative changes.

More recent evidence implies that the expectancy of life of a diabetic, after the development of stage three of proliferative changes, is but seven years. During these seven years it appears that kidney and other pathology become so severe as to be incompatible with life.

The characteristic vascular lesion of diabetic retinopathy consists of great numbers of minute saccular aneurysms in the retinal capillaries. These lesions were formerly called deep hemorrhages. Often the aneurysms are hyalinized. Two possibilities come to mind in regard to their formation: increased capillary pressure or histochemical changes that allow for the development of these aneurysms. In regard to the former, Friedenwald noted in studying histologic specimens of diabetic retinopathy, that localized retinal venous occlusions were associated with abundant newly formed capillary collaterals. Aneurysms were not seen in these newly formed vessels, suggesting that increased capillary pressure is not in itself sufficient to cause the aneurysmal dilations. Some abnormal weakness of the wall appears to be essential.

There are some who feel that the retinal microaneurysms, are actually abortive neovascular buds, arising in response to a vaso-formative factor, much as in the embryologic vascular developments, where a pre-ordained normal supply of vaso-formative factor insures an orderly development of the retinal vascular tree.

Today it is finally accepted that the picture of dia-

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betic retinopathy is not dependent on hypertension, arteriosclerosis, or atherosclerosis. The retinal lesions of the diabetic are closely related to the renal lesions described by Kimmelsteil and Wilson. The latter are often associated with capillary aneurysms in the kidney glomerulus. The typical globular hyalin, glomerular nodule of Kimmelsteil and Wilson may be in fact, a hyalinized saccular capillary aneurysm, showing the retinal and renal lesions to be joint manifestations of the same vascular disease. Ashton and Friedenwald found no distinguishing features in staining and histochemistry between hyalin of the Kimmelsteil-Wilson nodule and the thickened walls of the retinal capillary aneurysm. Both have well developed membranes. No other organs have as yet shown these hyalin nodules other than a rare one that has been seen in the brain.

Frequently it is difficult to ascertain the exact "age of onset" of mild diabetes. By "age of onset" we usually mean "age of first detection", and assume the possibility of a slightly longer period of duration. Since capillary aneurysms are so seldom seen in conditions other than "diabetes of long duration," the presence of these aneurysms is assumed to indicate changes due to diabetes, and the diagnosis of "diabetic retinopathy" is justified. Various estimates have been made relating the onset of capillary aneurysms to the duration of the disease, and vary from "50 per cent of individuals having aneurysms with a duration of sixteen years of diabetes, to an incidence of 95 per cent of individuals expected to have aneurysms with a duration of twenty years of diabetes." Very seldom a patient is seen who has a duration of as long as thirty years and with no retinal aneurysms observed to be present.

When the Kimmelsteil-Wilson disease is sufficiently advanced, so that it may cause pathologic physiology, the hypertension and albuminuria findings are associated with numerous soft, white "cotton-wool exudates" (transudates) in the retina. During the next six or eight years it may be expected that such fundus pathology will continue to develop into stage three, proliferative retinopathy, and that the duration of life after reaching stage three retinopathy will be but seven years. During this interval gross hemorrhage into the vitreous may occur, and with accompanying changes, visual acuity may be reduced to light perception. It is difficult with many patients to attach an exact date of onset of diabetes, particularly if the disease is mild. Waite and Beetham have clearly illustrated the lack of correlation between the onset of hemorrhages (capillary aneurysms) and the NPN, fasting blood sugar, or insulin requirement, the systolic and diastolic blood pressures, or other features of diabetes.

I share the opinion of many ophthalmologists who attest that all diabetics will develop capillary aneurysms if they live long enough.

The peak age incidence of diabetes is between forty and sixty years. Modern medical care of diabetes allows a life expectancy for the diabetic to be estimated at "three-fourths of that of the normal individual of that age." A more accurate estimate might be made if it were related to the age of onset of the disease. If the age of onset is as late as sixty years of life, the diabetes should have less influence on life expectancy than if the age of onset is in childhood. It is expected that most diabetics will, within twenty years' duration after the onset of diabetes, develop aneurysms in the retina, and that one out of every six with aneurysms will eventually live to become blind. Probably in no field of blindness statistics is there greater difficulty in obtaining accurate incidence figures, for the reason that these persons have a medical course of gross hemorrhage into the eye, followed by partial clearing, and again followed by massive hemorrhage. These individuals, even though reduced to mere light perception, live in the hope that there will again be clearing which will enable them to become independent. No category of blind persons is more reluctant to admit of their condition, and frequently these individuals are represented by an age group which requires that they remain at home, dependent upon family custody.

Notwithstanding the exceedingly great progress made in the detection and treatment of diabetes, retinal hemorrhages and proliferative changes still occur, with a duration of disease onset, as predicted by Waite and Beetham in 1935.

Retinal pathology as viewed with the ophthalmoscope is in no way altered from the earliest descriptions made 100 years ago, following the invention of the ophthalmoscope by Helmholz.

In the brief twenty-five years, during which I have been in the practice of ophthalmology, I have seen a generation of diabetics develop the disease, strive to obtain the best possible medical care for the diabetes, and now to be losing their sight from retinal hemorrhages. I am now as unable to do anything of value, to prevent the natural progress of this blindness, as when I terminated my ophthalmic residency. It is with extreme regret that I anticipate the second generation of diabetics in my practice, still as limited in preventive therapeutic advice to stop recurring retinal hemorrhages, once they have developed, as were the early observers, who first described so carefully these changes.

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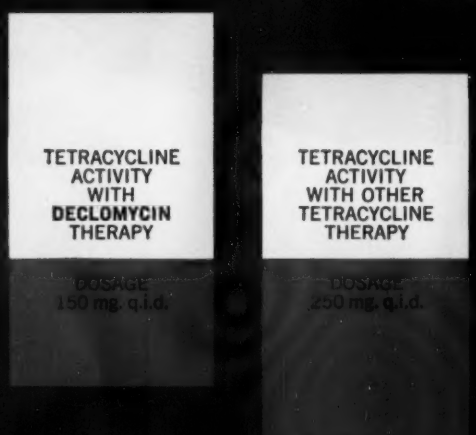
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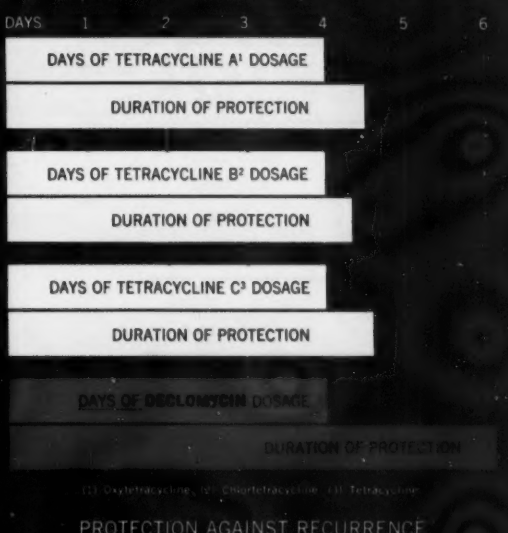
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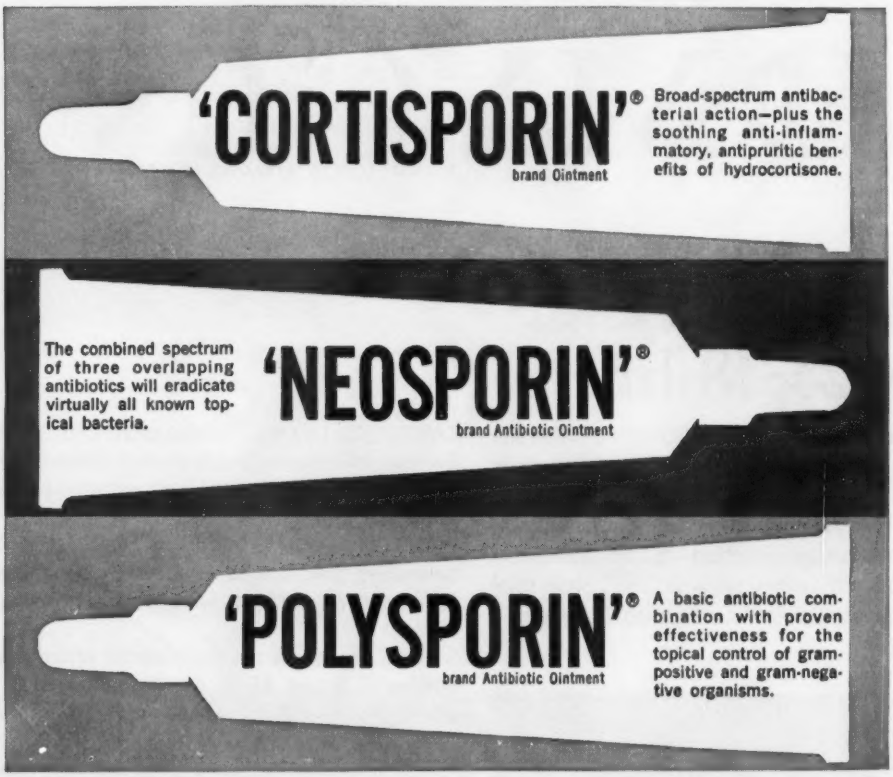
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What Can Be Expected of the Glucose Tolerance Test?

Raymond E. Fuller, M.D.
Grand Rapids, Michigan

DURING our recent survey of glucose tolerance tests it became apparent that confusion still exists as to what the test measures and what information the test will yield. The glucose tolerance test can give only restricted information about carbohydrate metabolism. Clinicians, however, frequently draw unwarranted conclusions from it. A general disregard for proper conditions necessary to assure reliable and reproducible results was noted. For these reasons, it seems timely to review the physiology, interpretation and indications for the glucose tolerance test.

Physiology

Glucose tolerance can be defined as the maximum amount of glucose the body can dispose of in a unit of time without disturbing the homeostasis of the body. Three principle factors are involved in the disposal of glucose given for a tolerance test: (1) hepatic regulation of the blood sugar by release or storage of glucose, (2) increased peripheral utilization, and (3) increased glycogen storage in both muscle and liver.

Soskin[1] believes that hepatic regulation is one of the most important factors. When the blood sugar is increased rapidly by a glucose load, the liver decreases the rate of glucose release and rapidly stores glucose as glycogen (glycogenesis). At this time there is a marked difference between blood glucose in the portal and in the hepatic veins. In depancreatized dogs whose blood sugar has been stabilized with a constant insulin drip, an intravenous glucose load will produce a normal "tolerance curve;" but in hepatectomized dogs whose blood sugar has been stabilized with a constant glucose drip, an intravenous glucose load will produce a "diabetic tolerance curve."[1,2] Normal glucose tolerance curves—but at a higher level—are produced in a Houssay animal (pancreatectomized and hypophysectomized).[1,2] Therefore, in the experimental animal a normal glucose tolerance curve may occur in the absence of insulin. In clinical practice, a great number of variables are measured other than the ability of the patient to produce insulin after a glucose load. The total patient must be considered whenever a glucose tolerance test is performed.

Factors Affecting the Glucose Tolerance Test

The ability of the body to dispose of a glucose load depends on the integrity of the liver and pancreatic islets, the state of the peripheral tissues, and other modifying conditions. The role of the liver and pancreas has been mentioned.

The state of the peripheral tissues is influenced by activity. The beneficial effect of exercise is well known.[3] Blotner[4] reported an adverse effect of inactivity on glucose tolerance. Sixty-three of seventy adults were found to have decreased glucose tolerance during prolonged inactivity. On retesting those patients who returned to activity, Blotner found the tolerance improved or normal. Prolonged malnutrition or starvation decreases glucose tolerance.[5] Carbohydrate tolerance has been shown to be decreased in the aged by most investigators.[6,7,8] Mosenthal,[9] testing healthy ambulatory subjects, found no decreased tolerance in the aged. It has been suggested that the relative physical inactivity in the elderly accounts for the decreased carbohydrate tolerance.[4]

Various endocrine diseases may modify the body's response to a glucose load.[2,10] Hyperthyroidism increases the rate of gastrointestinal absorption of glucose, resulting in early high curves by the oral glucose

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tolerance test. Hypothyroidism causes decreased rate of absorption of glucose with resultant low or flat curves. Macho,[11] studying glucose tolerance in thyroid disease by intravenous glucose tolerance, found normal or increased tolerance in hyperthyroidism and decreased tolerance in the hypothyroid patients. The tolerances improved in the hypothyroid patients after treatment with desiccated thyroid.

The effect of hyperadrenocorticism (Cushing's syndrome) is one of increasing the rate of gastrointestinal absorption of glucose and increasing peripheral insulin resistance. In Addison's disease there is decreased absorption of glucose and increased insulin sensitivity as measured by the insulin tolerance test. It has been shown by Burns et al[12] that cortisone acetate (200 mg.-400 mg.) by mouth is followed by elevation of the blood sugar within four hours in both healthy and ill subjects. Chronic administration of cortisone to healthy subjects causes an elevation of fasting blood sugars, but this effect wears off in about seven days. Ill subjects pretreated with a single dose of 200 mg. of cortisone showed a significantly greater impairment of glucose tolerance and greater insulin resistance than did normal subjects treated with cortisone. Burns concluded that there is an interaction between stress and adrenal hormones in modifying carbohydrate metabolism. The effect of steroids is an indirect one, making the subject more responsive to stress. Fajans and Conn[13] found that cortisone increased the sensitivity of the oral glucose tolerance test in patients with "borderline" curves and in patients with "latent" or "pre" diabetes. They selected a dose of 62.5 mg. of cortisone given eight and a half and two hours before the glucose tolerance test. (If the patient weighs less than one hundred sixty pounds, 50 mg. of cortisone is given.) In their hands this amount gives the fewest false positives in normal persons. In a follow-up of thirty-four individuals (relatives of diabetic patients) with positive cortisone glucose tolerance tests, ten developed diabetes or prediabetes within six years; whereas in fifty-seven individuals (relatives of diabetic patients) with negative cortisone glucose tolerance tests, only one developed diabetes within this time. Others found similar results using ACTH.[14]

Decreased glucose tolerance has been noted with pheochromocytoma, neoplasia,[15] fever, inflammation and other stress,[3] uremia,[16] various psychiatric conditions,[17,18] in the immediate postoperative period[19] and postpartum period,[20] and in a host of other medical and surgical conditions.[3,21,22,23,24,25] Most of these can be seen to be associated with stress or increased levels of corticosteroids.

Indications for Glucose Tolerance Test

The test is indicated for the diagnosis of diabetes mellitus in patients where fasting blood sugars are normal. When the two-hour post-prandial blood sugar is above the level diagnostic for diabetes mellitus (in our laboratory, above 160 mg. per 100 ml. using serum glucose measurements on an autoanalyzer), we are willing to establish the diagnosis of diabetes mellitus on this basis alone; hence do not resort to the glucose tolerance test in this situation. It is also used for the screening of relatives of diabetic patients[13] and the screening of patients with the "prediabetic state" as suggested by: fetal giantism,[26] perinatal mortality (late fetal and neonatal deaths), rapidly developing obesity especially after pregnancy, and temporary diabetes during any acute stress.[27,28] Any glycosuria must be considered diabetes mellitus until proved otherwise and many times the glucose tolerance test will be the court of last resort.

The test may be indicated in patients presenting with retinal vascular changes and peripheral neuropathies of undetermined etiology, in patients with furunculosis, non-healing wounds and non-healing fractures, xanthosis, carotinodermia, and in certain other conditions occasionally associated with diabetes, for example, gout and carcinoma of the fundus of the uterus.[28]

When extended to five hours, the test is helpful in the investigation of the patient with spontaneous hypoglycemia.[29] It must be remembered that reactive hypoglycemia is occasionally associated with early diabetes mellitus.[13,28]

The glucose tolerance test is not indicated in patients with persistently elevated fasting blood sugars and in established diabetes mellitus, because the test does not quantitate the severity of the disease or mode of therapy. The oral glucose tolerance test may be difficult to interpret in conditions which disturb the tolerance curves due to variability in gastrointestinal absorption of glucose such as: hypo- and hyperthyroidism, Cushing's disease, Addison's disease, intestinal malabsorption diseases, and postoperative conditions such as gastrectomy and gastroenterostomy. Zollinger and Hoerr[24] showed that postgastrectomy and gastroenterostomy patients have abnormally rapid glucose absorption due to the rapid emptying of food into the jejunum. This resulted in early high curves followed by hypoglycemia in two to three hours.

Conditions of the Test

For reproducibility of results and to facilitate ease of interpretation, the test must be done under stand-

ardized conditions. Much of the unreliability of the oral glucose tolerance test stems from the failure to standardize the conditions of the test.

A preparatory diet of 300 gms. carbohydrate for a minimum of three days is considered essential.[5,13] Conn[5] showed that patients with prolonged malnutrition may need more than five days of high carbohydrate feeding to effect a complete return of normal carbohydrate tolerance. Wilkerson[30] recently published data on the effect of various preparatory diets on glucose tolerance of healthy men and women. He suggested that the importance of the 300 gm. carbohydrate diet is exaggerated. In criticism of this view, his subjects were all healthy and previously were fed on institutional diets (high in carbohydrate). The longest period on a restrictive diet was seven days, and still these subjects on the 50 gm. carbohydrate diet showed significant elevations of the one-hour blood sugar, although admittedly still within normal limits. While many of Wilkerson's points are well taken, dietary standardization seems advisable to us.

The patient when tested should be twelve to fourteen hours post absorptive. The test should be performed in the morning with the patient near basal conditions.

Other factors that clinicians should try at time of test to standardize or consider so that its interpretation is facilitated are: physical activity, fear and other emotional influences, body posture during the test (recumbency tends to delay gastric emptying), the concentration and dose of glucose solution administered (highly concentrated solutions delay gastric emptying), and fever or even the mildest infection such as a cold.[23] As stated previously, carbohydrate tolerance is decreased during time of acute stress (fever, inflammation, surgery or trauma) and in the immediate post stress period so that no valid interpretation can be drawn from the test unless it is carried out after the period of acute stress has passed.

Technical factors that should be standardized are the site of the blood sampling (capillary blood sugars are higher and less reliable then venous), and the method used for the blood glucose determination.[20] In comparing the Folin-Wu and Somogyi-Nelson (true glucose) methods on venous blood, Mosenthal[9] found fewer false positives by the latter. This is due to the variable amounts of non-glucose reducing substances included in the Folin-Wu method.

The use of certain drugs may also affect the glucose tolerance curve. Anti-cholinergic drugs may slow gastric emptying time. Sedatives, hypnotics and salicylates in large doses have been shown to affect the curves.[20] The effect of steroids has been mentioned.

Test and Criteria for Interpretation

The test most useful in clinical practice is the three-hour oral glucose tolerance test. Although we believe the two-hour value after the loading dose of glucose is the key value, the three-hour value may be of some help in estimating the severity of the metabolic disturbance in cases showing delayed curves at two hours.

TABLE I. UPPER LIMITS OF NORMAL FOR VENOUS BLOOD BY THE ORAL GLUCOSE TOLERANCE TEST

	FBS	Peak	2 Hours	Probable Diabetic 2 Hours
Fajans & Conn (13) (Somogyi-Nelson)	110	160	110	110-120
Mosenthal (9) (Somogyi-Nelson)	100	150	100	100-110
Moyer & Womack (31) (Folin-Wu)	120	170	125	125-140

The test is performed by giving the patient 100 gm. (or 1.75 gm./kg.) of glucose in 500 cc. of chilled lemon flavored solution after the fasting blood sugar is drawn. Blood sugars are drawn at hourly intervals for three hours following the glucose load. Some investigators also draw a ninety minute specimen, but this is not necessary in a great majority of tests unless a rebound is suspected at two hours. Blood sugar determinations are obtained by the Somogyi-Nelson method. If the Folin-Wu method is used, the above limitations should be kept in mind. We find the criteria of Fajans and Conn[13] to be the most satisfactory (Table I).

A peak venous blood glucose of greater than 160 mg./100 ml. and a two-hour blood sugar of 120 mg./100 ml. or greater is diagnostic of diabetes mellitus. A "probable diabetic curve" would be a one-hour value of 160 mg./100 ml., a ninety minute value of 135 mg./100 ml. or above, and a two-hour value between 110-120 mg./100 ml. A peak blood sugar above 160 mg./100 ml. in itself is not significant if the remainder of the curve falls within normal limits. The two-hour blood sugar is the critical value. Fajans and Conn[13] state that terminal hypoglycemia occurring three to five hours after a glucose load in individuals who exhibit mildly abnormal curves should reinforce one's suspicion of early diabetes mellitus rather than rule it out.

Reliability and Reproducibility

Mirsky[32] has stated that anyone can be labelled diabetic if a sufficient number of oral glucose tolerance tests are performed. Soskin[1] goes so far as to state that

the oral glucose tolerance test has no practical value. Unger,[33] in screening apparently healthy subjects, found that sixty out of one hundred fifty-two had two hour blood sugars over 110 mg. per cent (Mosenthal's criteria). Forty-nine patients were retested with only 75 per cent reproducible results. In contrast, Wilkerson,[20] screening large numbers of pregnant women, found a high degree of specificity and sensitivity. Fajans and Conn,[13] testing one hundred twenty-seven healthy subjects without family history of diabetes or large babies, found only one diagnostic curve and one probable curve. If specific controls are adhered to as stated above, the test will give consistent results.

The Intravenous Glucose Tolerance Test

Because of the alleged variability of the oral glucose tolerance test as cited above, and because of the uncertain gastrointestinal absorption of glucose in some conditions, some investigators have championed the use of the intravenous glucose tolerance test.[1,25,29]

In favor of the test, if standardized, it is reliable, reproducible, and it gives sharp distinction between mild diabetes and normals.

Arguments against the intravenous test are: a greater number of blood samples are needed, an intravenous injection is required, and it is likely that the intravenous introduction of glucose into the body is less physiological than its absorption into the portal system.[29]

There is at present no standardized intravenous method. The rapid method (25 gm. of glucose given in four to five minutes) is becoming more popular.[25,34,35] The intravenous tolerance test, like the oral glucose tolerance test, does not detect blood glucose flow in and out of the glucose pool so that abnormalities in which two antagonistic processes are occurring simultaneously may be missed, for example, in a Houssay animal.

The intravenous glucose tolerance test is indicated in those conditions that affect glucose absorption from the gastrointestinal tract such as: postgastrectomy and gastroenterostomy, hyper- and hypothyroidism, Cushing's disease, Addison's disease, and in intestinal malabsorption defects. The most common reason for using the intravenous method is nausea with an oral glucose load.

Summary

1. The oral glucose tolerance test is a useful and reliable clinical test if performed under proper standardized conditions and if interpreted in the light of the patient's total condition.

2. In the detection of diabetes, it is not necessary to draw blood samples for longer than three hours. The two-hour specimen is the critical point of the test.

3. In functional hypoglycemia, the five-hour oral test is preferred.

4. In certain conditions affecting gastrointestinal absorption of glucose, the intravenous test should be used.

5. Each doctor or group should use one test consistently and thus gain experience interpreting data from it.

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Hypertension Causes

F. James Conway, M.D., of the Hypertension Unit at The University of Michigan Medical Center, reports that about one person in five will have high blood pressure (hypertension) in later life, but medical science does not know why.

"Certain disorders of the kidneys and endocrine glands cause a few cases of high blood pressure; however, we never identify an actual cause in most patients."

Salt, fatty diets, and the rush and stress of modern life all seem to contribute to hypertension, he said. "Although each has been blamed for causing the disease, nobody has been able to prove it."

Dr. Conway made these statements over a radio broadcast co-sponsored by the State Medical Society and the U-M Medical Center.

"The person who leads a rushed and harrassed life will aggravate a hypertensive disorder," Dr. Conway pointed out. "Over-weight also causes greater suffering from high blood pressure. But neither stress nor overweight nor heavy salt diets by themselves will cause the disease."

The Intravenous Tolbutamide Response Test

Initial Observations

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William L. Lowrie, M.D.
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THE STANDARD oral and intravenous glucose tolerance tests are widely used to establish the diagnosis of diabetes mellitus when random blood sugar values are normal. The ability to assess glucose tolerance by other means would be helpful. An alternate method would permit greater diagnostic confidence in borderline cases. This is particularly true since some have questioned the validity of the glucose tolerance test.[1] Everyone agrees that a shorter test would be preferable.

The advent of the oral hypoglycemic agents has altered therapeutic approaches and has stimulated clinical investigation in diabetes. Mirsky and co-workers[2] noted that the hypoglycemic response to oral tolbutamide differed when the patient with diabetes was compared to the patient without diabetes. The hypoglycemic response in the latter was rapid and transient; while the response in the patient with diabetes showed a more gradual decline. Following the administration of intravenous tolbutamide, Unger and associates[3] have been able to separate patients with diabetes from those without diabetes with reasonable accuracy. Barros Barreto and Recant[4] have applied this test more recently to the detection of the "pre-diabetic."

This paper records our initial observations with the "intravenous tolbutamide response test." We were obliged to determine our own criteria of responsiveness, since the method of measuring the blood specimens for glucose used by us differed from that of Unger.

Method

In the fasting state, one gram of sodium tolbutamide* dissolved in 10 ml. of sterile distilled water is injected intravenously over a two-minute period. Blood for glucose is drawn prior to and at twenty and thirty minutes after the injection. At thirty minutes the test is terminated and the patient is given 15 grams of carbohydrate orally. Serum is analyzed for glucose by a modification of the method of Hoffman,[5] using the autoanalyzer.[6] In our laboratory a fasting serum glucose under 130 milligrams per 100 ml. is considered normal.

Sixty-six patients have been tested. Twenty-nine have diabetes and thirty-seven are free of diabetes. All patients with diabetes were sufficiently mild to require dietary therapy only. Prior to the intravenous tolbutamide test, the exact status of glucose tolerance in each case was determined. Standard glucose tolerance tests were performed in the majority of the non-diabetics and in many of the patients with diabetes. The status of glucose tolerance in some patients was established by multiple post-prandial determinations of serum glucose. Each patient consumed a standard 300-gram carbohydrate diet for three days prior to the intravenous tolbutamide test. All patients were ambulatory, afebrile and free of acute stress when the test was performed. The patients without diabetes had fasting serum specimens for glucose ranging from 65-120 milligrams per 100 ml. with an average of 82 milligrams per 100 ml. The average fasting serum glucose in the group with diabetes was 117 milligrams per 100 ml. with a range of 75-200 milligrams per 100 ml. Eight patients with diabetes had fasting levels of serum glucose above 130 milligrams per 100 ml. No patient received more than one test.

Results

Figure 1 presents the percentile fall of serum glucose in both groups at twenty and thirty minutes following the injection of sodium tolbutamide. The mean percentile fall in serum glucose from the fasting level in the group without diabetes was 29 per cent (range of +10 to —69 per cent) at twenty minutes and 35 per cent (range —13 to —74 per cent) at thirty minutes. In the group with diabetes, the mean percentile fall in serum glucose was 9 per cent (range of +4 to —27 per cent) at twenty minutes and 14 per cent (range of 0 to —42 per cent) at thirty minutes.

A study of Figure 1 suggests that a 20 percentile fall in serum glucose thirty minutes following the injection of tolbutamide will separate maximally the

From the Division of Metabolic Diseases, Henry Ford Hospital, Detroit, Michigan.

*We are indebted to the Upjohn Company, Kalamazoo, Michigan, for the generous supply of sodium tolbutamide.

study group with diabetes from the one without diabetes. The wide range of results at twenty minutes in the non-diabetic group vitiates this specimen, even though 80 per cent of results in the diabetic group show a fall of less than 20 per cent. However, at thirty minutes, thirty-four of thirty-seven patients without diabetes showed a fall in serum glucose of greater than 20 per cent; while twenty-one of twenty-nine patients with diabetes showed a fall in serum glucose of less than 20 per cent.

The decrease in serum glucose in milligrams per 100 ml. at twenty and thirty minutes was studied. No separation of the two groups was noted. The absolute levels of serum glucose in milligrams per 100 ml. at twenty and thirty minutes were then analyzed. Thirty-six of thirty-seven patients without diabetes had a serum glucose level below 80 milligrams per 100 ml. at both twenty and thirty minutes. In the diabetic group, twenty-two of twenty-nine patients had levels of serum glucose above 80 milligrams per 100 ml. at both twenty and thirty minutes. These interesting results are tempered by the fact that the average fasting level of serum glucose in the non-diabetic group was 82 milligrams per 100 ml.; while 117 milligrams per 100 ml. was the average fasting level in the group with diabetes. Ten patients with diabetes had fasting levels of serum glucose below 100 milligrams per 100 ml. Eight of these had serum glucose levels below 80 milligrams per 100 ml. at either twenty or thirty minutes. The percentile fall in serum glucose from the fasting level is the best way of expressing results and effecting separation of the two groups.

The accuracy of interpretation of our results is based upon two assumptions. First, the initial analysis of glucose tolerance by standard methods is accurate; and second, the 20 percentile line at thirty minutes gives maximal separation. We believe the first assumption to be highly accurate; thus those patients in the non-diabetic group are truly free from diabetes and likewise for the diabetic group. Ultimately a rigid division in percentile fall in serum glucose from the fasting level between the non-diabetic and diabetic groups may not stand. However, for purposes of simplicity in this study we have arbitrarily chosen it as the maximal point of separation. With the accumulation of more experience with this test, a range of separation between the diabetic result and the non-diabetic result may well evolve. Indeed, a range of separation may be preferable. Using the 20 percentile fall thirty minutes after tolbutamide as the dividing line between diabetic and non-diabetic, those cases with a fall of greater than 20 per cent should be free of diabetes, while those cases with a fall of less than 20 per cent should have diabetes. As mentioned above, thirty-four of thirty-seven patients without

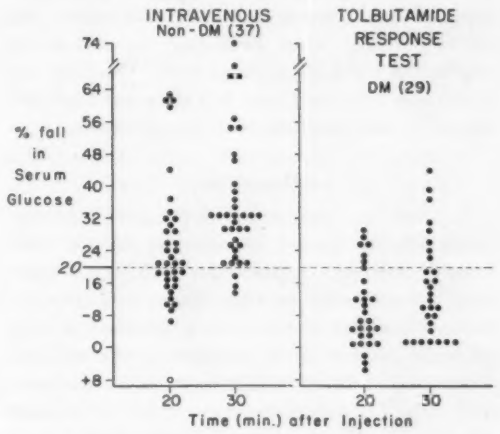

Fig. 1. Percentile fall in serum glucose at twenty and thirty minutes following the intravenous injection of one gram of sodium tolbutamide.

diabetes showed a fall in serum glucose of more than 20 per cent at thirty minutes. Hence there were three false positive results (non-diabetics whose fall in serum glucose was less than 20 per cent). In the group with diabetes, twenty-one of twenty-nine cases showed a fall in serum glucose at thirty minutes of less than 20 per cent. Eight cases in this group had false negative results (diabetics whose fall in serum glucose was more than 20 per cent).

Analysis of False Results

False positive results: All three patients without diabetes whose serum glucose fell less than 20 per cent from the fasting level had true false positive tests. All had perfectly normal glucose tolerance tests prior to the intravenous tolbutamide test.

False negative results: The eight patients with false negative results are interesting. Three patients had true false negative responses. Their glucose tolerance tests were diabetic in type, yet at thirty minutes the fall in serum glucose was greater than 20 per cent of the initial level. The tolbutamide test in a fourth patient was performed incorrectly. This test was done three hours post-prandially rather than in the fasting, post-absorptive state. The other four patients with false negative results were known diabetics who were

in remission at the time of the study. These patients with mild diabetes had been able to convert an abnormal glucose tolerance test (in the past) to normal through rigid weight control. At the time of the tolbutamide test, these patients had normal glucose tolerance. These patients show compatible rather than contrary results when comparing the tolbutamide response and glucose tolerance tests. Therefore, out of sixty-six tests, there were only three true false positive results and three true false negative results.

Discussion

Any test that measures insulin activity indirectly, as do both the glucose tolerance test and the intravenous tolbutamide response test, will yield a specificity and sensitivity less than 100 per cent. It seems reasonable to pursue a test with a specificity of three true false positives out of thirty-seven cases and with a sensitivity of three true false negatives out of twenty-nine cases. The clinical usefulness of any test depends upon its ease of performance and safety as well as its inherent validity. The oral glucose tolerance test is perfectly safe but many times is inconvenient because of its duration. The vagaries of intestinal absorption including the vomiting of the test dose of glucose may lead to problems of interpretation. The intravenous glucose tolerance test is too cumbersome for general use and is no shorter than the oral variety. The thirty-minute intravenous tolbutamide test overcomes many of these objections. Its technique is simple. It is brief. Prolonging the test to one to two hours, as has been suggested,[7] seems to rob it of one of its main advantages—brevity. We have no data to show the effect of prolongation of the test on its accuracy, but we believe that if two hours is to be spent, one might as well use the glucose tolerance test. Of course, much more experience is necessary with this test before we can substitute it for a glucose tolerance test with confidence. Many times the intravenous tolbutamide response test will be used in conjunction with the glucose tolerance test to improve the diagnostic accuracy in a given clinical problem. Nevertheless, with confidence established in the accuracy of the tolbutamide test, one can easily visualize its substitution for the standard glucose tolerance test.

We believe the safety factor of this test is good. Up to the present time, we have had no untoward toxic, allergic or anaphylactoid reactions. Hypoglycemia during the test has been no problem. As a precaution we give 15 grams of carbohydrate at the end of the test. We do not give intravenous tolbutamide to any person with known sulfonamide sensitivity.

Based on our present experience, we believe the intravenous tolbutamide response test deserves further study. With only six false results out of sixty-six cases, it seems reasonable to continue an analysis of the test. We plan to continue the present technique, eliminating the twenty-minute specimen as sensitive enough but much too non-specific to be rewarding. The 20 percentile fall will be used as the separation point between patients with and without diabetes until further study indicates the need for a change in criteria. As mentioned earlier, a broader zone of separation may be necessary. With present knowledge and experience, it should be perfectly clear that we cannot diagnose diabetes with this test. We can only compare our results with accepted standards. Further experience will either bolster our confidence in this test or dictate its abandonment. If its present sensitivity and specificity are confirmed, one can easily visualize ultimate usefulness with appropriate clinical problems.

Summary

The serum glucose response to one gram of sodium tolbutamide intravenously was analyzed in sixty-six patients, twenty-nine with diabetes and thirty-seven without diabetes. Thirty-four of thirty-seven patients without diabetes had a fall in serum glucose thirty minutes after injection of greater than 20 per cent; while twenty-one of twenty-nine patients with diabetes had a fall in serum glucose of less than 20 per cent. Analysis of false results showed three true false positive results and three true false negative results. Further observations are necessary to firmly establish the value of this test as a diagnostic aid for mild diabetes mellitus. The initial results are encouraging.

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The Federal Government and the Nation's Health

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I AM PLEASED and honored to have been invited to meet with you today and to have the privilege of reviewing certain aspects of the place of the Federal Government in the health of the Nation. I do this from a strong conviction of the need for physicians everywhere to have more opportunity to view medicine and its problems from a broad vantage point—something which I know from my own experience is difficult to achieve in competition with the multitude of problems which require one's immediate attention in the day-to-day practice of medicine.

With the exception of a flurry of health activities in the World War I period, the Federal Government played a very limited role in family and community health until about the period of the thirties. During the First World War, for example, the Public Health Service was authorized to provide extracantonment sanitation activities and to inaugurate a venereal disease control program. And when the disastrous pandemic of influenza hit the United States in 1918-19, the Congress appropriated $1 million to the Public Health Service to help suppress this disease.

In the postwar period, however, Federal health activities languished. Then the great depression of the early thirties brought the Social Security Act, which set the stage for much greater participation in public health activities. For the first time, a substantial program of grants-in-aid to the States for health purposes was authorized. Appropriations were made first for general public health activities. Later, specialized programs, such as tuberculosis control, were added. The national venereal disease control program was renewed and strengthened by legislation in 1938.

Despite these measures, the Federal investment in public health and medical research was quite meager until the beginning of World War II. In 1940, for example, a year in which the Federal budget was $6.2 billion, only $3 million was spent for medical research and an additional $19 million for all other health purposes, including grants to the States. This was just nineteen years ago, a period very fresh in the minds of many of us in this room.

With the onset of World War II, and the disastrous influenza pandemic of 1918 far from forgotten, there evolved wide realization of the vital roles that individual and collective health could and would play in the national security. In the early days of World War II there was quick recognition on the part of the Federal Government that a healthy citizenry was vital to winning the war and that a bold attack on the prevention and cure of disease must have stimulus, as well as supplementary financial support, from the Federal Government to enable the country's investigative resources to fulfill their greatest potential.

There was thus established a cooperative approach to medical research on the part of universities, foundations, industries, private citizens and government at local, state and Federal level which it is expected will continue to be the pattern for this country for years to come.

It is hardly necessary to recount the details of what has happened in medicine in the past decade and a half as a result of this cooperative approach to medical research, which had its initial big impetus in the context of a great war. Probably never before in history has there been such an extraordinary accumulation of new medical knowledge and the technological ability to apply this knowledge.

It has been pointed out by Franklin Murphy, as well

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as others, that medicine, being a blend of the physical and natural sciences on the one hand and of the social sciences on the other, has been affected profoundly by the socio-economic as well as by the scientific revolution through which we have been passing in this country since the mid-1940's. Frankly, I am afraid that few of us have fully recognized the magnitude of these socio-economic changes, cognizant as all physicians are of the scientific advances in medicine.

As contrasted with the situation which existed prior to World War II, we now have in America a citizenry keenly interested in health and broadly aware of what now is available in medicine—a citizenry which, through its dimes and dollars, is contributing to all sorts of disease oriented foundations. Furthermore, we have a citizenry which not only expects the search for new medical knowledge to go forward at an even greater pace, but which also will insist increasingly that the great advances in medicine somehow be made available to all of its people.

So much for background.

I would like to talk about many of the numerous and important areas of health interest in the Department of Health, Education, and Welfare. In deference to time and my listeners, however, I will simply highlight several of our current major concerns: medical research, medical education, medical care and international health.

Expenditures for medical research from all sources are at an all-time high in the United States, and this year will be in excess of $500 million. Parenthetically, this sum represents a little less than 4 per cent of the more than $12 billion which our country will invest this year on total research and development.

Although medical research is at an all-time high, there is no doubt that it must be pursued even more vigorously in the future. While many of our serious health problems have come under control, new and more complex ones constantly are arising to be added to those as yet unsolved, such as cancer, heart disease, the degenerative diseases of our aging population, and many others. Some of these new problems are fostered by the way we live. Industrial and suburban growth bring further problems, such as air and water pollution. Very much in the forefront is the job of protecting our population against the hazards of radiation.

As many of you know, a group of distinguished consultants under the chairmanship of Dr. Stanhope Bayne-Jones last June reported the results of their study of medical research and education for former Secretary Folsom. This group then predicted that the current annual national expenditures for medical research would increase to a level approximating a billion dollars by 1970 but warned of the critical problem of professional manpower.

Well-trained professional people in ever larger numbers are going to be needed not only to conduct the search for new knowledge but to bring this knowledge in the form of better medical care to our rapidly expanding population. Speaking to this point, the Bayne-Jones group also reported that: "A minimum of fourteen and as many as twenty new medical schools will have to be built (by 1970) if the existing number of physicians per 100,000 population is not to fall."

Because of the critical nature of the medical manpower problem, and because the Bayne-Jones group concerned itself primarily with medical research, Surgeon General Burney recently appointed another group of consultants to look more closely into the whole question of needs for physicians and to explore ways in which these needs may be met.

The results of this study, which should be completed by the end of August,* combined with the results of an intensive study of twenty medical schools recently completed by the National Institutes of Health and the Bayne-Jones report together should provide a strong basis from which to develop national goals for medical research and medical education for the years ahead. Once these goals have been established, it will be necessary to determine the proper division of responsibility for their achievement as between government at Federal, State and local levels on the one hand and industry and philanthropy on the other. Certainly, unless there is a substantial increase in the production of physicians and other professional health personnel not only the total research effort but the health services of the Nation will be severely hampered in the years ahead.

Of course, the best knowledge, personnel and hospitals in the world will accomplish little if our people cannot afford to pay for the medical care they need. Although we have reached new heights of prosperity in the United States, medical costs represent a serious problem to many American families. In 1957, for example, 44 per cent of all families in this country had incomes below $5,000 and one family in nine had an income below $2,000. Furthermore, as many as one-quarter of all American families today have no cash savings, and in 1958 it was estimated that more than half of our families had savings of less than $500. For these people the costs of long-term and other disabling

*Report of the Surgeon General's Consultants on Medical Education, "Physicians for a Growing America," Public Health Service Publication No. 709, September 15, 1959.

illness can be a crushing burden, particularly if the victim is the breadwinner.

The present administration is convinced that voluntary health insurance represents the best means of helping most people meet the costs of medical care within our traditional American free enterprise system.

Preliminary estimates for December 1958 show that just over 121 million people, or 70 per cent of the population, have some form of hospital insurance. Ten years earlier, in December 1947, the 53 million persons with such protection had represented 37 per cent of the total population.

Insurance against the costs of hospital care is the most widely held type of health insurance. Most, but not all, persons having such coverage also have insurance against some other medical costs. At the end of 1957, 190 million persons—65 per cent of the population—carried surgical care insurance as compared with 18 per cent at the end of 1947.

Insurance covering the costs of physicians' services for other than surgical care increased even more sharply, from 6 per cent at the end of 1947 to 43 per cent, or 72 million, of the population in 1957. Much of this form of insurance, of course, applies only to physicians' visits to hospitalized patients. The 72 million persons with regular medical expense insurance in 1957 included approximately 13 million with major medical expense policies, a form of insurance unknown a decade ago.

In spite of rapid advances in the recent past, the gaps in coverage still are wide. For example, a problem of major importance is that which befalls the worker whose health insurance coverage is included among the fringe benefits of his employment and who loses such coverage during long periods of forced unemployment.

Of particular concern to everyone right now are the serious gaps in coverage of our older citizens, less than half of whom are covered by any kind of health insurance. Heartening recognition is being given to this problem by the American Medical Association, the American Hospital Association, the American Nursing Home Association, the Blue Cross, the Blue Shield and the insurance industry.

From statistics now available—and there is usually at least a year's lapse between actual accomplishment and the availability of statistics to bear out the accomplishment—health insurance coverage for the aged has increased at a fairly steady rate, amounting to between two and two and one-half percentage points a year since 1952. Later statistics may show that this rate has stepped up in the past year.

In any event, are we moving fast enough? There are now 15 million people in this country who are sixty-five years of age and over, and in a very few years there will be 20 million. Older persons have larger than average medical care needs. As a group they use about two and one-half times as much hospital care as the average for the whole population. Their incomes are considerably lower than those of the rest of the population and in many cases are either fixed or declining in amount.

Because both the number and the proportion of older persons in the community are increasing, a satisfactory solution to the problem of providing and paying for adequate medical care for the aged will become more, rather than less, important.

In our society the existence of a problem does not necessarily indicate that action by the Federal Government is either necessary or desirable. This particular problem does, however, merit close attention by the Federal Government, government at state and local level, the medical profession and all others concerned. Public interest has resulted in the introduction in Congress of a number of bills which would provide hospitalization and other medical care benefits to the aged through the Social Security mechanism. At the conclusion of hearings on various Social Security amendments last summer the House Ways and Means Committee asked the Secretary of Health, Education, and Welfare to make a study of alternative ways of providing insurance against the cost of hospital and nursing home care for old-age, survivors and disability insurance beneficiaries. It was my privilege to serve as chairman of the task force set up by the Secretary to make this study. The study is just about finished and the report will be turned over to the Chairman of the House Ways and Means Committee in the very near future.**

In this report the Department takes no position either for or against government intervention. The report is a comprehensive factual document which we believe will be of considerable assistance to us, to the Committee and to all others concerned with the problems which led to the study.

It is obvious that the health needs of the elderly will be taken care of in one way or another. Private, voluntary and local resources are capable of a major contribution toward meeting them. Even though the pressures for action at higher levels of government will

**"Hospitalization Insurance for OASDI Beneficiaries"—Report submitted to the Committee on Ways and Means by the Secretary of Health, Education and Welfare on April 3, 1959.

continue to mount, and even though more comprehensive programs ultimately may prove necessary, we should in any case do everything in our power to strengthen these private, voluntary and local efforts. However one may feel about the necessity for broader State and Federal responsibility, he surely cannot believe that the results would be all gain.

Ability to pay for medical services relates, of course, to the cost of these services, which now are at an all-time high—especially hospital services.

We must continually increase our efforts to keep people well, which efforts cost the country far less in the aggregate than caring for them after they are ill. We must also look toward a better distribution and utilization of expensive and highly skilled personnel.

There is a need to keep people out of hospital beds if at all possible; to make more intelligent use of existing hospitals and other medical care facilities; and to plan future facilities with imagination so that the design and operations are better suited to the needs of the patients to be served.

One of the ways in which we are hopeful of holding the costs of medical care to a minimum is by reorienting care to the particular needs of the individual patient, as, for example, in the progressive or graduated care programs now under intensive study by the Public Health Service. The plan for a general hospital is to divide the patient units into three "zones of care:" a special care unit for patients who are critically ill (sometimes called intensive care units), an intermediate care unit for those who are less critically ill, and a self-care unit for ambulatory patients.

In addition to these three general divisions in the hospital, a comprehensive graduated care plan would include an adjoining unit for long-term care, a chronic disease unit, and a home-care program.

Several advantages have been claimed for these plans: better patient care in a shorter period of time, more effective use of medical and nursing staffs, greater satisfaction for patients, family, physicians and nurses, and, hopefully, as was said before, lower costs to the patient.

The Public Health Service very shortly will publish its initial studies in the whole area of progressive patient care.

Finally, in addition to its concern with domestic health affairs, the Federal Government has a very active interest in the field of international health. In his January 9, 1959, address on the State of the Union the President pointed out that "to advance the cause of freedom we must do much more than help build sound economies" and that "the spiritual, intellectual, and physical strength of people throughout the world will in the last analysis determine their willingness and their ability to resist communism."

This year nearly $100 million will be spent in the field of international health. The following listing indicates the broad scope of the activities supported by these funds.

1. Contributions to the World Health Organization, the Pan-American Health Organization, UNICEF and the United Nations.

2. The world-wide malaria eradication program and assistance to underdeveloped countries in improving community water supplies.

3. Health activities carried out through the International Cooperation Administration under technical assistance agreements with about forty other governments.

4. The research and training grant programs of the National Institutes of Health, which extend overseas as well as across the Nation itself.

There is little question but that collaborative efforts to improve the health of peoples throughout the world provide a real opportunity for reducing world tensions and promoting the cause of world peace and economic security.

In closing, I want to emphasize that the basic aim of the Federal Government in health affairs is that of a partner—a partner with the health professions, educational institutions, foundations, industry, and all levels of government. It is a partner which tries to encourage individual initiative. It is a partner which is attempting to make possible a vigorous and continuing attack on our health problems to the end that we may continue to make gains in the unending war against disease and disability.

"It is an axiom of philosophy that nothing in this world is either altogether bad or altogether good. Pity, the tenderest, the most natural, the most useful of the virtues, is not at all times in place either with the soldier or the priest; both with the priest and the soldier, there are occasions when it must be held in restraint—when confronted by the enemy, for instance. Officers do not make a practice of recommending it on the eve of battle, and in some old book I have read that Monsieur Nicole held it in distrust as the motive principle of concupiscence."—"Manuscript of a Village Doctor," ANATOLE FRANCE.

Immunization of Infants with Quadruple Antigens

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THE USE OF a triple vaccine (DPT) for protection of children against diphtheria, pertussis and tetanus has been accepted practice for some years. The effectiveness of a killed trivalent poliomyelitis vaccine has been demonstrated. The possibility of incorporating four antigens (DPT + polio) in one preparation for vaccination against all four diseases has been a subject of considerable interest because its use obviously would simplify administrative procedure. Results of tests in animals reported by Kendrick and Brown[1] suggested that a combined product had promise and deserved serious study. Recent studies in children with such a product (Quadrigen) by Barrett et al,[2,3] demonstrated immune response of the injected children to each of the four antigens. The results support the reasonableness of the procedure; and they underline the importance of adding data from other areas obtained under different conditions. In the present study, a report is made of observations on a small group of children in the University of Michigan Pediatric Clinic.

Material

1. The quadruple vaccine contained concentrates of the components for each antigen (poliomyelitis, diphtheria, tetanus and pertussis) so that a fully effective dose of each would be present in the 0.5 cc. inoculum.[4] The potency of each component in the vaccine was determined by the standard test procedures prescribed by the Division of Biologic Standards of the National Institutes of Health (NIH). Each individual antigen after combination met or exceeded minimum requirements established for monovalent vaccines.[4-8]

The group of subjects in which the quadruple vaccine was studied consisted of fifty children who were in good health and had received no prior immunizations. Seven of the infants at the start of immunization were two months old, thirty-three were three months of age and eight were four months old. Two children were sixteen months and four and one-half years respectively. Forty-three of the mothers had received poliomyelitis vaccination within two years of the birth of their children. The infants were injected with the quadruple vaccine on the same schedule adopted by the routine Well Baby Clinic program for the standard DPT and poliomyelitis vaccine. Prior to inoculation a blood sample was obtained, and then three monthly injections of 0.5 cc. quadruple vaccine were given intramuscularly. Two to four weeks after the final injection a blood specimen was obtained. Thirty subjects were given a fourth dose of the quadruple vaccine nine to ten months following the primary dose and a blood specimen was obtained two to four weeks later. An additional group of thirty children who were originally part of the study are not included in this report because of insufficient collection of specimens. Blood was obtained to permit testing for poliovirus antibodies (Types I, II, and III), diphtheria and tetanus antitoxin, and pertussis agglutinin. The poliovirus antibody determinations and pertussis agglutinin titers were conducted by the Department of Epidemiology of the School of Public Health, University of Michigan. Tests for diphtheria and tetanus antitoxin were performed according to accepted procedures by the Research Laboratories of Parke, Davis and Company.

Results and Comments

Reactions.—There were no serious untoward reactions following the immunization procedures. Parents were instructed to report any illness and the children

Quadruple antigens were supplied as "Quadrigen" by Parke, Davis and Co. This project was supported by a grant from Parke, Davis and Co.

From the Department of Pediatrics and Communicable Diseases, University of Michigan Medical Center. The assays of all blood specimens for poliomyelitis antibodies and pertussis antibody were performed in the Department of Epidemiology, University of Michigan School of Public Health by Drs. Gordon C. Brown and Pearl L. Kendrick, respectively. Data presented in this report will be part of a larger study to be published at a later date by Doctors Brown and Kendrick. Assays of the sera for diphtheria and tetanus and antibodies were done in Research Laboratories of Parke, Davis and Co., by Dr. E. A. Timm.

were checked at the time of each clinic visit to ascertain any systemic reactions encountered. Eighteen of the group had a mild febrile reaction with less than two degrees of temperature elevation and did not require any therapy. Three patients had a moderate febrile reaction of more than two degrees of temperature elevation persisting from twenty-four to seventy-two hours and requiring aspirin administration. No history of vomiting, diarrhea, convulsions or paralysis was elicited. Three had mild local discomfort at the site of injection lasting less than twenty-four hours. No persistent nodules were seen and no rash was observed.

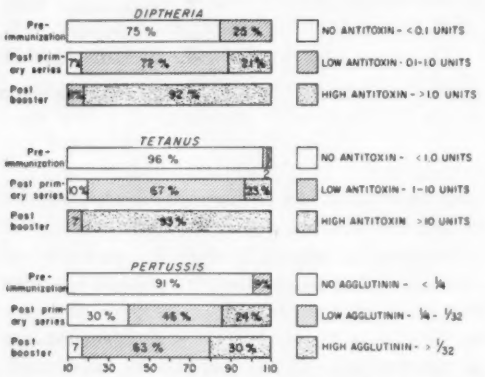

Fig. 1. Response of patients to the diphtheria, tetanus and persussis antigen in Quadrigen. It will be noted that before immunization 25 per cent of these children, mostly two to three month old infants, had low diphtheria antibody levels, 4 per cent had tetanus antibodies and 9 per cent agglutinins against pertussis. Following immunization there was good response to all three antigens. Following the booster dose at twelve months of age, all children had diphtheria antibodies, all had tetanus antibodies, and 93 per cent had agglutinins against pertussis.

The general health of these children was excellent. There were two children with mild eczema who were placed on allergy diets (these children had strong family history of allergy). None of the children had any serious illness during the period of study and four children had mild surgical problems (umbilical hernia, inquinal hernia). All children received complete health supervision by one of the authors during the eighteen months they were studied.

Pre-immunization Antibody Titers.—The fifty pre-immunization blood specimens were tested for polio myelitis neutralizing bodies, diphtheria and tetanus antitoxin levels and pertussis agglutination titers (Fig. 1). In regards to the latter three antigens, 25 per cent of the group had diphtheria antitoxin levels of greater than 0.1 units per cubic centimetres of serum. Four per cent had greater than 1.0 units per cubic centimetres of serum tetanus antitoxin and 9 per cent of the serums had demonstrable pertussis titers.

As noted, most of the mothers of the infants had received prior poliomyelitis immunization and this is reflected in that only five children were triple negative for poliomyelitis (triple negative—less than one to four antibody titers against all three types). It is of interest that there was no apparent correlation between the time of the mother's vaccination and the level of antibodies at the time of the first blood samples.

By type 38 per cent (19) of the infants were negative to Type I, 42 per cent (21) had a low titer of antibody (from 1:4 to 1:32) and 20 per cent (10) had a high titer (greater than 1:32).

Twenty-four per cent (12) of the infants were negative to Type II, 40 per cent (20) had a low titer and 36 per cent (18) had high titer antibody levels.

To Type III, 44 per cent (22) had no demonstrable titer, 36 per cent (18) had a low titer, and 20 per cent (10) had a high level.

Response to Primary Immunization.—After the completion of the primary series of three 0.5 cc. inoculations, 93 per cent of the infants had responded to diphtheria, and 90 per cent to tetanus with a good protective level of antitoxin. Seventy per cent had a titer of 1:4 or greater on testing for pertussis agglutinins. (The pertussis agglutinins were actually 1:20 or greater, see note in legend of Fig. 1.) The overall polio response revealed that 62 per cent of the infants had significant titers to Type I, 84 per cent to Type II and 76 per cent to Type III. The remainder had negative titers (Figs. 1 and 2).

In regards to pre-immunization titers, of the nineteen subjects originally negative to Type I 42 per cent (8) showed a significant response. Of the twelve originally negative to Type II, 92 per cent (11) developed titers greater than 1:4 and there were 82 per cent (18) of the twenty-two originally negative to Type III who had a good response.

Comparison of those with initial low titers of antibodies revealed that 48 per cent (10) of the twenty-one had significant levels remaining to Type I, 65 per cent (13) of the twenty with low titers to Type II had adequate levels remaining and 43 per cent (8) of the eighteen with low titer to Type II had levels greater than 1:4.

Of interest is the response of those subjects with initial high titers. Seven of the ten with high titers (1:32 or more) to Type I had levels fall to 1:8 to 1:16 and only one subject still had a high titer. Seventy-eight per cent (14) of those with high titer initially to Type II had levels greater than 1:4 following the primary series. However, all these titers except two were moderately lower than initial levels. Ninety per cent (8) of the ten with high initial levels to Type III had significant titers, but again, in all but one subject this represented a drop in titer.

Response to Fourth Injection.—Of the thirty children who received an additional booster of the vaccine nine to ten months after their primary series, the response to the diphtheria and tetanus antigen were excellent with 100 per cent showing protective levels. Pertussis results revealed that 93 per cent had protective agglutinin levels.

In regards to poliomyelitis, it is noted that 57 per cent had adequate levels against Type I, 87 per cent had significant titer against Type II and 77 per cent had measurable titers against Type III. In this group of children, unlike following the primary series, there was little correlation between the pre-immunization and post booster titers.

Discussion

The quadruple vaccine was shown to present no difficulty in administration and there were no severe untoward reactions. Certainly the use of only 0.5 cc. inoculum volume was a decided advantage.

In regards to diphtheria and tetanus, it was shown that excellent responses were evoked. Pertussis response following immunization was significant, although not as effective as the former two antigens.

Note.—In the interpretation of pertussis agglutination titers, it should be pointed out that the small volume, concentrated antigen, rapid test[9] was used and the final serum titers as given here are approximately one-fifth those that would be obtained in the one ml. test. For example, a titer of 1:64 in the test used here would be equivalent to 1:320 in the 1 ml. test.

Poliomyelitis antibody level determinations revealed that the vaccine contained potent antigens capable of evoking excellent responses. Type I was less effective in this study than the other two types in evoking a response, but in individual cases excellent titers were obtainable.

In those infants with high initial poliomyelitis titers, post-primary series antibody levels were less than those obtained in infants with initially low titers. The explanation of this fact may be that it reflects crowding out phenomena[10] or it may be that an adequate antibody response was evoked but masked by initial maternal antibodies.[11] Further studies are being carried out by Doctors Brown and Kendrick to elucidate this problem. Related to this problem is the finding that a considerable number of infants had no demonstrable antibody levels to the poliomyelitis viruses after completing the primary immunization series. Thirty-eight per cent had negligible levels to Type I, 16 per cent had no demonstrable level to Type II and 24 per cent were without significant level to Type III. After a booster dose in thirty subjects, it is to be noted that 43 per cent of the infants had no demonstrable levels of antibody titers against Type I, 13 per cent against Type II and 23 per cent against Type III. Thus there seems to be a certain percentage of infants who do not develop and maintain a significant antibody titer against the poliomyelitis viruses with the routine immunization program when it is started in early infancy.

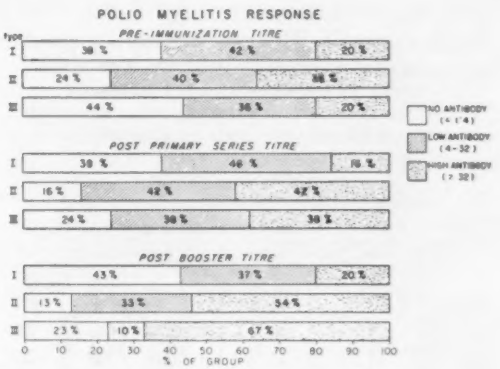

Fig. 2. Response to poliomyelitis antigen in Quadrigen. It is significant that following the booster dose at twelve months of age 43 per cent had no antibodies against Type I, 13 per cent had none against Type II, and 23 per cent none against Type III poliomyelitis viruses. As pointed out in the text, this would indicate the need for additional boosters at a later date.

These results, however, should be considered in relationship to data obtained in infants who have had no poliomyelitis vaccine. This data has been collected in Detroit, Michigan, by Barrett et al, and they found that infants age six to eight months had very low protection against Type I and III and less than 50

per cent had significant titer for Type II. Thus these results when compared to the findings in the immunized group in the study clearly show the effectiveness of the Quadrigen vaccine following the primary series (Table I).

TABLE I. POLIOMYELITIS ANTIBODY TITERS. COMPARISON OF POLIOMYELITIS ANTIBODY TITER IN INFANTS AGE SIX TO EIGHT MONTHS FOLLOWING PRIMARY IMMUNIZATION WITH QUADRIGEN AND IN A GROUP OF SIX TO EIGHT-MONTH-OLD INFANTS RECEIVING NO VACCINE

	Present Study: Six to Eight-Month-Old Infants Response Following Primary Series			Unvaccinated Six to Eight-Month-Old Infants (Barrett et al.)		
	I %	II %	III %	I %	II %	III %
No titer (<184)	38	16	24	80	50	90
Low titer (1:4-1:32)	46	42	33	20	35	10
High titer (>1:32)	16	42	33	0	15	0

In regard to the results following the booster injection, comparison should be made with the findings in unvaccinated one-year-old children and in those infants initially vaccinated after six months of age. It can be seen from Table II that the results in the present study are less than that in the latter group but significantly higher than in the unvaccinated group.

TABLE II. POLIOMYELITIS ANTIBODY TITERS. COMPARISON OF POST BOOSTER TITER IN PRESENT STUDY TO UNVACCINATED INFANTS OF SAME AGE AND TO INFANTS IMMUNIZED AFTER SIX MONTHS OF AGE WHO HAVE RECEIVED A BOOSTER

	Present Study: Twelve to Fourteen-Month-Old Infants Following Booster			Boosters Infants Over Six Months When Immunized (Barrett et al.)			Unvaccinated Twelve to Fourteen-Month-Old Infants (Barrett et al.)		
	I %	II %	III %	I %	II %	III %	I %	II %	III %
No titer	43	13	23	0	3	3	75	60	80
Low titer	37	33	10	20	2	12	5	35	15
High titer	20	54	67	80	95	20	20	5	5

In view of the above findings, the conclusion can be made that very young infants are capable of responding to the quadruple vaccine but that an additional booster (or boosters) will need to be given to those infants immunized prior to six months of age. One method suggested by Barrett et al was to give four injections in the primary series followed by a booster one year later. An additional method may be to give a booster again in the second year. Clinical experience has indicated the wisdom of immunizing infants as early as possible because of the severity of poliomyelitis and pertussis in infants under six months of age.

Summary

This study was carried out in order to test the effectiveness of a recently developed quadruple vaccine incorporating poliomyelitis, diphtheria, tetanus and pertussis antigens.

A group of fifty children (forty-eight infants less than four months of age) received the vaccine as part of the routine Well Baby Clinic program and there were no serious untoward reactions noted. This quadruple vaccine is shown to be a potent antigen capable of evoking responses to all four antigens. Discussion is presented concerning the need for additional booster injections in those infants whose immunization began before six months of age.

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Effectiveness of Resins in the Treatment of Hyperkalemia

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HYPERKALEMIA of sufficient degree to interfere with myocardial function is a major cause of death in acute renal insufficiency. Potassium intoxication occurs in this disease when oliguria is prolonged or when there is an accelerated rate of tissue breakdown causing an increased release of potassium into the extracellular fluid. In the treatment of life-endangering hyperkalemia, intravenously administered hypertonic sodium salts exert an immediate action but this effect is of short duration. The use of insulin and a hypertonic glucose solution will control potassium intoxication as long as twelve hours. Beyond this length of time some form of dialysis or lavage has been required to lower the serum potassium concentration. During the past few years, reports have appeared of the efficacy of cation exchange resins in controlling hyperkalemia. Many of these have been concerned with the use of hydrogen and ammonium cycle resins.[1,2,3] More recently sodium cycle resins have been utilized.[4,5,6,7] This study describes further experience with a sodium cycle carboxylic acid resin* in fifteen patients with renal failure.

Mode of Action and Methods of Administration

A cation exchange resin is a synthetic polymer, each fraction of which contains a functional group (COO^-, SO_3^-, et cetera). The cation attached to such a group is exchangeable for another cation in the surrounding solution (gastric or intestinal secretion) depending upon the relative affinity of the two ions for the exchange position, the concentration of cations concerned (both on the resin and in the solution), and the pH of the medium.[8]

The sodium cycle potassium-free cation exchange resin, while passing along the intestinal tract, will exchange the sodium ions on its functional groups for potassium ions. Calcium and magnesium ions are also removed.[8,9] Removal of potassium from the gastrointestinal juices lowers the potassium concentration in the extracellular fluid and plasma. Resins are insoluble and are not absorbed so that potassium ions which have become attached to the resin are effectively sequestered from the pool of exchangeable body potassium until they are actually eliminated in the feces.

Resins may be given either by retention enema or orally. If given by enema, 20 gms. in 200 ml. water are used. The enema should be retained for at least ninety minutes in order for maximum exchange to take place. This amount may be administered every two hours if necessary. Any water retained in the body from the enema must be included as part of the daily fluid intake.

If the patient can tolerate oral feedings, administration of the resin by this route appears to be more effective. The resin may be mixed with sugar and lemon flavor, adding just enough water so that it can be swallowed. It can also be mixed with butter and sugar to make butterballs. This has the advantage of administering the resin with a minimum amount of water. Two grams of resin can readily be incorporated into each butterball. Usually 20 to 40 grams of resin per day will control hyperkalemia, but if potassium intoxication is threatening more may be necessary. In such instances, it may be given both rectally and orally. The amount of resin required depends upon the degree of hyperkalemia present and the rate at which the serum potassium is rising.

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*Carboxylic Acid Type Resin (Sodium Salt) supplied by Eli Lilly and Co.

THE AUTHOR
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Rarely is more than 150 grams of resin needed in twenty-four hours. In these fifteen patients, no nausea or vomiting was noted that could be ascribed to the resin, nor were fecal impactions or diarrhea encountered.

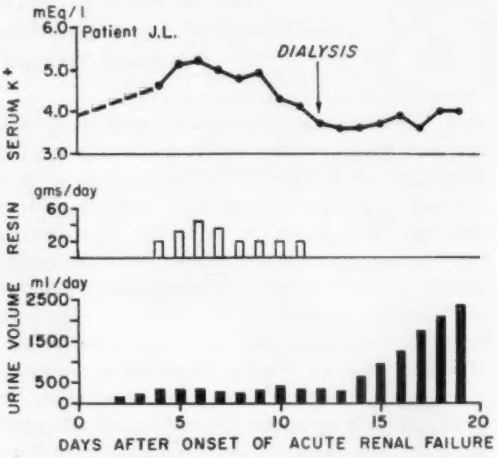

Fig. 1. Control of the serum potassium level with sodium cycle resin in patient J. L., who developed acute renal failure from a transfusion reaction.

Clinical Material

Eleven patients with acute renal failure, two patients with terminal chronic pyelonephritis, and two patients with terminal chronic glomerulonephritis, have been given this resin to control hyperkalemia. Some of these when first seen required the acute administration of insulin and intravenous hypertonic glucose and/or sodium salts because of impending potassium intoxication. However, after resin therapy had been instituted, dialysis for the control of hyperkalemia was not necessary, nor was any other means of controlling the serum potassium concentration required. The following selected cases illustrate various aspects of the use of resin.

Patient J. L., a twenty-five-year-old woman, received two pints of incompatible blood during a Caesarian section. Approximately sixteen hours later she was noted to be icteric. She developed acute renal failure with a fourteen-day period of oliguria. From the fourth to eleventh days of her illness, the patient received daily 20 grams of resin orally plus additional resin by retention enema for the prevention of hyperkalemia (Fig. 1). She was able to tolerate the oral resin in spite of nausea being present. The serum potassium was never over 5.2 mEq./L. Hemodialysis was performed on the twelfth day because of the severity of the uremic symptoms. Recovery was uneventful following the onset of diuresis.

Patient M. C., a nineteen-year-old boy, received a severe injury to his right lower extremity when it was crushed by an overturned tractor. He lay in the field for nine hours before the accident was discovered. Acute renal failure followed with a twenty-day oliguric phase. The serum potassium was 6.9 mEq./L. on the day following the injury and fell to 5.7 mEq./L. in twelve hours after the rectal and oral administration of resin. The resin was then given orally in butterballs. It is to be noted that this patient quite rapidly developed hypokalemia even during the oliguric phase (Fig. 2). This is remarkable in view of the large mass of muscle which was damaged and the extensive hematoma present. Dialysis was performed on the thirteenth day because of uremic symptoms. Diuresis began on the twentieth day and recovery followed, although a permanent residual peripheral neuropathy of the right leg remained.

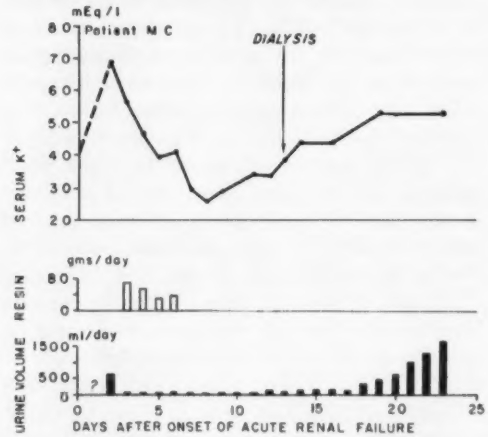

Fig. 2. Lowering an elevated serum potassium concentration to below the normal range by use of the sodium cycle resin in patient M. C., who had acute renal insufficiency subsequent to a crush injury.

Patient L. B., a thirty-six-year-old man, suffered a crushing injury to his right leg when a heavy metal door fell, trapping him for forty-five minutes. The femoral artery was transected but the vessel was plugged with a bone fragment which prevented exsanguination. A graft was inserted in the arterial defect. The patient was hypotensive for several hours both before and after surgery. Acute renal failure ensued with a prolonged oliguric phase. Oral resin was started on the third day because of a serum potassium of 7.1 mEq./L. Seventy grams of resin were given in twenty-four hours. The serum potassium fell promptly to 5.1 mEq./L. and remained in the normal range even after discontinuance of the resin. He died of overwhelming infection on the twentieth day (Fig. 3).

Patient M.B., a fifty-year-old man, had chronic pyelonephritis. Cystectomy and ureterosigmoid transplantation for carcinoma of the urinary bladder had been performed four years previously. He entered the hospital because of persistent vomiting. He was very dehydrated and there was marked weakness and lethargy. The blood NPN was 132 mgm. per

100 ml. and the serum potassium was 8.7 mEq./L. During the twelve hours following admission, 260 grams of resin were given by the oral and rectal routes. Intravenous fluids were administered and the urinary output increased. The serum potassium dropped to 5.4 mEq./L. during this period (Fig. 4). The patient died of uremia on the thirteenth day following admission. Postmortem examination confirmed the presence of bilateral renal staghorn calculi and disclosed a right perinephric abscess.

Discussion

Hyperkalemia was controlled or was prevented from developing in all patients by the use of this resin. Since this type of resin has been utilized, hemodialysis solely for the treatment of potassium intoxication has

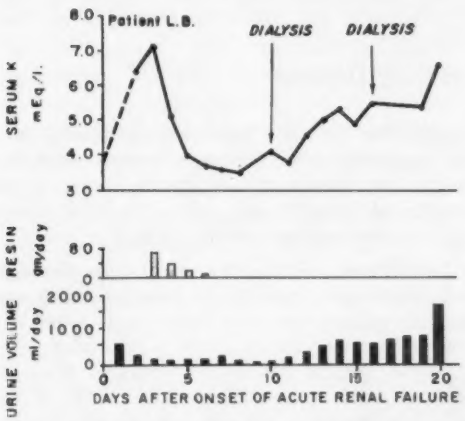

Fig. 3. Prompt reduction of threatening hyperkalemia with orally administered sodium cycle resin during the oliguria of acute renal failure in patient L.B.

not been necessary. Some patients have developed hypokalemia from resin therapy during the oliguric phase of acute renal failure (Fig. 2). Cessation of its administration when the serum potassium goes below 5 mEq./L. will probably prevent this occurence. In using cation exchange resins, care must be exercised to avoid accentuation of the hypokalemia which is sometimes present during the diuretic phase of acute renal failure. It is exceedingly important that these resins should not be used for a continuous period of time in patients with chronic renal disease because of the danger of causing potassium depletion.

A tendency toward hypernatremia has been noted in some patients. This is because the resin donates sodium as it removes potassium. The resin used in this study contains approximately 6 mEq. of sodium per gram of resin. No serum sodium concentration over 155 mEq./L has been noted. A greater danger than hypernatremia would be the expansion of the extracellular fluid volume by the sodium derived from the resin with subsequent edema formation or congestive heart failure. This has not occurred in any of our patients, however, when using this resin very careful attention must be given to restricting the daily total fluid intake.

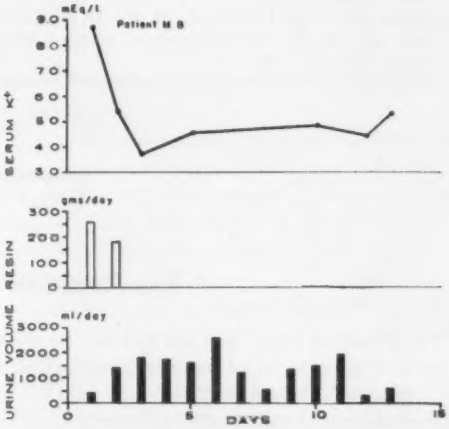

Fig. 4. Effective treatment of severe hyperkalemia with the sodium cycle resin in patient M.B., who had terminal chronic pyelonephritis.

As orally administered resin readily removes hydrogen ions from the upper gastrointestinal tract secretions, there is usually some alleviation of the metabolic acidosis which is the result of impairment of renal function. This is in contrast to the hydrogen and ammonium cycle resins which aggravate acidosis by introducing these ions into the body. Although cation exchange rations may remove significant quantities of calcium and magnesium, tetany was not noted in any of these patients.

Summary

The sodium cycle carboxylic acid cation exchange resin has been effective in preventing or controlling hyperkalemia in fifteen patients with renal failure. It is superior to the hydrogen and ammonium cycle resins in the treatment of this condition. The use of the sodium cycle resin constitutes a distinct advance in the treatment of threatening potassium intoxication and obviates the necessity of dialysis for this indication.

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The Physician's Role in Civil Defense

"The Physician's Role in Civil Defense" was one of the interesting topics at the recent regional meeting of the AMA Council on National Security's Committee on Disaster Medical Care in Washington, D. C.

Discussing this subject was C. J. Wagner, M.D., chief of the Division of Health Mobilization, U. S. Public Health Service.

Based on the findings and calculations made during the 1959 Operation Alert exercise, Doctor Wagner described and summarized the problem 30 days post-attack as follows:

(1) the supply of physicians is insufficient and will remain so, even if each nurse, dentist, and veterinarian is counted as equivalent to a physician,

(2) the number of available hospital beds is grossly inadequate. Even though the professional manpower is also limited, there remains a capability to use effectively several times the remaining hospital beds; and

(3) medical supplies and equipment are grossly inadequate, poorly distributed, and limit the extent to which hospital bed shortages can be corrected by improvision.

Conclusions drawn from this analysis, 30 days post-attack, reveal the medical situation to be desperate but not necessarily hopeless, he said.

"The basic problems are the immediacy and magnitude of the medical care and public health requirements. Almost instantaneously, millions of casualties are in need of treatment. Not only is there a gross disparity between the medical patient load and the available health resources of manpower, supplies, and facilities, but there is a corresponding disparity in all the supporting services, such as transportation, fire and rescue, communications, et cetera. Finally, the radiological fallout in many areas will delay or prevent any organized medical activity for days or weeks."

Dr. Wagner said the first role of the physician, then, is to make it possible for these patients to treat themselves—meet their own health needs—until local conditions permit the physician to treat them. The American Medical Association recognized this problem and made it possible for the Public Health Service to initiate a self-help research project. This will consist of a standardized procedures manual related to a standardized medical kit for use by the layman in self, family, and neighbor care. It will emphasize, in addition to general medical care, hygiene and sanitation, simple methods to be used in the treatment of shock burns, fractures, and hemorrhages, as well as simplified nursing techniques. All these necessary efforts have the purpose of preserving life until the physician can catch up with the patient load.

Once the methods to be used and the medical kit contents are agreed upon, the physician must take an active aggressive role in teaching the layman to use them. At the federal level, little can be done other than provide assistance as required to help the physician in this responsibility. Training aids can be developed and provided, the assignment of personnel to the states and organizations, within appropriation limits, can be supported, and the PHS inactive reserve corps can be made available for use at the local level.

Medical and Neurological Management of the Patient with Cerebral Vascular Accident

Matthew S. Atkinson, M.D.
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"STROKE" and "CVA" are time-honored terms with the merits of established usage and the connotation of an acute neurological disturbance usually in a middle-aged or elderly person. "Stroke" is a good term as it has meaning for physician and layman alike and carries no pathological overtones. "CVA" or "cerebrovascular accident" seem inappropriately chosen, however, since they are employed by the medical profession and, while implying both localization and vascular etiology, lack the anatomical and pathological precision which are necessary if treatment is to be appropriate and adequate.

Broadly speaking, there are four common mechanisms, by which neurological disease of vascular origin are produced: (1) brain infarction or softening, (2) transient arterial insufficiency, (3) parenchymatous brain hemorrhage, and (4) subarachnoid hemorrhage. Infarction and parenchymatous hemorrhage invariably mean destruction of nervous tissue although the former much more often than not results in survival, while the latter usually means a fatal outcome. With arterial insufficiency and subarachnoid hemorrhage there need be no tissue destruction, hence no persisting functional deficit. Ultimate prognosis remains ominous, however, in the absence of specific treatment.

Brain softening is due to critical deprivation of metabolites, supplied via the bloodstream, the most constantly requisite of these metabolites being oxygen and glucose. Critical deprivation can be brought about by *in situ* thrombosis of an artery; by atherosclerotic luminal narrowing without complete occlusion to the point where blood supply, initially merely inadequate to meet full tissue requirements (transient arterial insufficiency), later becomes inadequate to support tissue existence; and by embolic arterial occlusion. Since treatment of these several modes of pathogenesis may require different measures, it is important for the physician to classify correctly each case prior to planning of therapy.

Self-evidently, arterial softening and insufficiency occur in relation to territories of arterial supply. Yet, the extent of involvement in any given case is a highly complex matter depending as it does upon individual variations in configuration of the circle of Willis, the state of vessels at a distance from the site of occlusion, oxygen carrying capacity of the arterial circulation, and blood sugar level, to mention only a few of the factors.

Certain points, nevertheless, merit attention. It has become increasingly clear that arterial occlusion or extreme stenosis outside the cranial cavity (that is, in internal carotid or vertebral arteries) is the major factor operative in producing a large number of softenings and insufficiency syndromes. Where occlusion or severe narrowing can be shown by angiography to have occurred in the neck, vascular surgery to restore adequate blood flow may become a primary consideration of treatment.

Interference with internal carotid circulation will produce its effects above the tentorium, spottily or in devastating fashion, in territory supplied by anterior and/or middle cerebral arteries. Practically, this means in cortex and subjacent white matter of frontal and parietal lobes, superior and convex surfaces of temporal lobe with subjacent white matter, insula, basal ganglia, and/or internal capsule. Obstruction to a vertebral artery may produce effects below the tentorium in brainstem and/or cerebellum, or when conditions are right, above the tentorium in occipital

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lobe, inferior and mesial portions of temporal lobe, or thalamus—portions fed by the posterior cerebral artery which usually derives its main source of supply via the vertebral-basilar circulation.

So as to avoid misconceptions it should be pointed out that the majority of softenings and insufficiency syndromes derive from pathology in vessels which are not surgically accessible, that is, cranial portions of internal carotid and vertebral arteries, basilar artery, anterior cerebral, middle cerebral or posterior cerebral artery, or a branch of one of these several vessels.

Parenchymatous brain hemorrhage is a condition which in most cases is associated with hypertensive vascular disease. This does not mean that the patient when first seen need be hypertensive because his blood pressure may have dropped as a result of his brain insult. Parenchymatous hemorrhage occurs in a supratentorial location about five times as often as infratentorially and has predilection in about three-quarters of cases for a locus of origin in either the basal gangliar region or thalamus of one side although encroachment upon internal and external capsules and centrum semiovale is common, along with rupture into the ventricular system and exitus.

When hemorrhage occurs below the tentorium, the primary site of bleeding is about equally divided between pons and midbrain, on the one hand, and cerebellum, on the other; and death usually ensues more quickly than in cerebral hemorrhage. In this connection, with the exceptions of an occasional massive pontine, hemorrhage and the blow-out of a large arterial aneurysm, vascular disease of the brain is not a cause of really sudden death, but rather is nearly always compatible with survival for a minimum of several hours.

Subarachnoid hemorrhage, which may on occasion be associated with bleeding into brain substance or softening consequent upon interference with blood supply to the parenchyma, is most commonly due to rupture of an arterial aneurysm, that is, a dilatation at a weak spot in one of the intracranial arteries ordinarily belonging to or stemming from the circle of Willis and usually located near a point of branching. These aneurysms tend to occur most often about the anterior portions of the circle, and the commonest sites are at the junction of the internal carotid and posterior communicating arteries, on the middle cerebral artery in the sylvian fissure, and on the anterior communicating artery. Subarachnoid hemorrhage statistically carries a mortality figure with each episode in the neighborhood of 40 per cent—serious indeed, but small in comparison with the corresponding figure of well above 90 per cent for primary hemorrhage into the brain.

It should be apparent from what has been said that in the acute stage of a stroke accurate diagnosis is a prerequisite to rational management in view of the variety of treatment measures which are available and the necessity for application of the correct regimen to the particular case. With a complete history (if this is obtainable) and a careful physical examination the physician can establish which pathological mechanism is causing the trouble in about 75 per cent of cases. Lumbar puncture should be helpful in an additional 10 to 15 per cent. The primary importance of lumbar puncture, however, is probably that it enables the physician to rule out infectious processes, such as fulminant meningitis, which can simulate say subarachnoid hemorrhage if the patient is stuporous and an adequate history cannot be elicited. It is generally advisable, and is not contraindicated in acute strokes except when one pupil is large and fixed to light or when there are decerebrate extensor spasms of the extremities. While the pathology of the insult can be diagnosed with a high degree of accuracy on the basis of clinical and lumbar puncture findings, correct anatomical localization and assessment of the extent of the lesion may be difficult or impossible prior to autopsy. Fortunately, this is unimportant in the early management of stroke patients except for those in whom disease of arteries in the neck or the presence of a suitably located aneurysm offer a chance for surgical treatment. In these circumstances arteriography will be an essential source of diagnostic information to the surgeon.

Most strokes which come to the physician's attention in the acute stages are associated with a degree of paralysis of one side of the body or impairment in state of consciousness. In addition to these manifestations, there may at times be disturbances in the patient's ability to feel sensory stimuli on the affected side, to see to the affected side, to speak, or to coordinate his movements. Further, he may complain of dizziness or double vision or inability to swallow to mention only a few of the manifold possibilities of symptomatology dependent upon specific neurological dysfunction.

There are, however, certain more general points which, if properly taken into consideration, will facilitate accurate diagnosis. First, brain softening and insufficiency lumped together are much commoner than parenchymatous and subarachnoid hemorrhage

although autopsy figures would indicate that the respective incidence as the principal cause of death is much more nearly equal. As already pointed out, this simply means that most patients with softening or insufficiency are statistically likely to survive a given episode, most patients with primary hemorrhage into brain substance are statistically likely to die, and patients with subarachnoid hemorrhage have more nearly an even chance as between survival and demise.

Secondly, softening and insufficiency tend to occur at a somewhat older age than either parenchymatous or subarachnoid hemorrhage although as we all know, young people may develop infarcts and very old people have hemorrhages.

The presence at onset of headache, vomiting, convulsions, and coma as well as physical findings of stiff neck, systolic blood pressure above 200, and fixed pupils all favor hemorrhage as opposed to primarily ischemic pathology. Yet a massive infarct in internal carotid or vertebral-basilar territory may produce most of these same phenomena so that a lumbar puncture (in absence of specific contraindications) may add helpful information for making the differential diagnosis between hemorrhage and softening. Other clinical points such as the presence of rheumatic heart disease with auricular fibrillation, indications of a recent or remote myocardial infarction, or an absent carotid pulse in the neck may prove crucial in establishing the diagnosis of infarction in such a patient and may indicate the necessity for energetic treatment measures which would not be called for in hemorrhage.

The differential diagnosis between primary brain hemorrhage and subarachnoid hemorrhage is facilitated by several considerations. Probably most important, the patient with hemorrhage into brain substance usually has a hemiplegia while the patient with uncomplicated subarachnoid bleeding does not. If the episode occurs in a young person without hypertension, the odds are strongly in favor of its being due to subarachnoid hemorrhage. The presence of hypertension, however, does not help much since it has a high incidence in both conditions.

One diagnoses insufficiency syndromes by history or findings of transient, reversible neurological dysfunction—temporary hemipareses, unilateral numbnesses, aphasias, losses of coordination, episodes of vertigo or diplopia, et cetera. Here the differential diagnosis becomes more complex because considerations such as migraine, disseminated sclerosis, subdural hematoma, and brain tumor, which also produce transitory disturbances, must be entertained.

Having recognized the nature of the insult, the physician can institute a program of optimum treatment. In all stroke patients who are stuporous or comatose, it goes without saying that there must be (1) insurance of an adequate airway, (2) treatment of any congestive heart failure or acute pulmonary edema, whether it be primary and thus a factor in etiology or secondary to depression of brainstem centers by the intracranial lesion, (3) provision for adequate nutritional, fluid, and electrolyte balance which is usually best maintained in the absence of vomiting by feeding through a Levine tube, (4) attention to the need for voiding by insertion of a retention catheter, (5) turning of the patient at least once every two hours, (6) treatment of any infection, (7) placing of a flat board at the foot of the patient's bed and a pillow beneath his paralyzed arm if he is hemiplegic.

In cases of softening and insufficiency, maintenance of adequate blood pressure is very important since any sharp drop in pressure will decrease cerebral blood flow and hence increase ischemia. Oxygen by tent will further help to minimize brain damage. In carotid insufficiency and acute occlusions, either thrombotic or embolic, if the pathology can be shown to be in the cervical portion of the artery, vascular surgery may become definite therapy. Anticoagulants can be safely instituted in the absence of hypertension and are clearly indicated in patients with insufficiency of any of the vessels although drug maintenance after the acute episode will require adequate medical supervision. It may be necessary to employ sedation and/or restraint for extreme restlessness, but agents likely to suppress respiration or blood pressure, for example, morphine or heavy doses of thorazine, should be avoided. There is some evidence that after recovery from the acute episode, the patient may benefit from a low-fat diet to minimize future atherogenesis.

In both primary brain hemorrhage and subarachnoid hemorrhage blood pressure should be judiciously lowered if there is serious hypertension. Here the primary therapeutic problem is prevention of bleeding more than tissue hypoxia, and elevated blood pressure fosters further hemorrhage.

Otherwise there is very little, except for the general measures already outlined, to offer to the patient with parenchymatous hemorrhage. Surgical evacuation of the hematoma may have a place in selected cases after there has been a considerable period of survival, but it has not been found to be generally warranted in the early stages when most patients die. Repeated lumbar punctures are contraindicated in primary brain

hemorrhage as they will promote herniation at the tentorial incisure and/or at the foramen magnum.

In subarachnoid hemorrhage, when the patient is conscious, he should be kept sedated with the minimum effective dosage of phenobarbital. An ice bag will help to alleviate headache though small doses of codeine may also be required; and while headache is extremely severe repetition of lumbar puncture may further prove beneficial. The patient should be kept flat on strict bed rest with feeding by attendants for at least the first two weeks after his acute bleeding episode. He may subsequently be elevated in bed to 45° and start to feed himself, but under no circumstances should he be taken off other full bed rest precautions in less than a month and probably not before six weeks.

At some point after the acute episode the patient should have the benefit of carotid angiography. Optimum timing for this procedure remains a matter of controversy, and the physician should exercise his discretion for the individual case in selecting the proper juncture for its performance. If arteriography discloses a surgically accessible aneurysm, the patient should go to operation at what is clinically judged to be the most propitious time. On occasion, when an aneurysm is not directly accessible surgically, ligation of the appropriate internal carotid artery in the neck may be the procedure of choice.

Finally, rehabilitation of the ordinary stroke patient should begin as soon as he is over the immediate consequences of his acute episode. This means that the person with softening should have daily passive movement exercises for his hemiplegic extremities, and be gotten up early. The physician must realize that cerebral damage may mean relatively specific intellectual and emotional damage; and while in truth a stroke victim is the same person that he was before his stroke, in many ways he may not be altogether that same person. These circumstances will require acceptance without over-acceptance by the patient as well as support and understanding from the family.

Implications of Child Diet Habits

It is better to let your child miss an occasional meal than to force it on him, say dietitians at The University of Michigan Medical Center. A happy, healthy child is usually eager for food if his eating procedure is treated in a matter-of-fact fashion.

Children who are too tired from play or excitement may have little desire to eat food. Some parents have the mistaken idea that over-tired children will eat more, but the U-M food specialists urge that children be given time to rest before meals so they can relax and enjoy mealtime.

Otherwise food can become a tool to seek attention. Often an unhappy child receives satisfaction from refusing to eat.

Forcing a child to eat may trigger a prejudice against the particular food served. It is far easier to prevent these food prejudices than to correct them, say the dietitians. The parents' responsibility should be to serve suitable food in a friendly, congenial atmosphere without undue worry about how much the child eats in a single meal.

National Politics and Medical Interests

Again the medical profession and their families, as a profession and as individuals must take an active part in national politics as well as national legislation. Basically and fundamentally the profession is and must be non-partisan. However, there are certain principles which we must favor and others which we must oppose.

One particular type of legislation is now a predominant threat to the private practice of medicine as we have known it. The profession quite generally has been opposed to the Forand-type legislation which proposes to put all beneficiaries of OASI under medical and hospital attention, regardless of need and at a 0.5 per cent increased rate of social security tax. Private insurance companies, as well as Blue Cross-Blue Shield, have established special insurance policies and certificates to take care of these elderly people. Already over 60 per cent of this group carry such insurance. At the present time, the dominant urge is to put them all under social security and even raise the taxable income level from $4,800 a year to what might be necessary to meet the added expenses.

A CAMPAIGN OPPOSING Forand-type programs and offering insurance type has covered tremendous numbers of people but has not allayed the drive which exploded this year into national politics. The medical profession supported the Mills Bill, which was passed by the House and the Senate in August. The bill, which will take care of the elderly persons without adding to the social security program, was signed into law by President Eisenhower on August 31.

Both political parties have held national conventions, have adopted platforms and selected their candidates. The post convention Congress has met, transacted essential business, and from the standpoint of the medical profession, did a very satisfactory job. Medical care for the needy aged is what we desired with help from the federal government regular tax source and not from social security.

The newly-elected Congress if so minded could still adopt social security, and one Presidential candidate has so promised.

Every member should cast his ballot carefully on November 8, 1960.

Congressional Action

The last session of the present Upper House of Congress which met after the convention, had three care-for-the-aged bills to consider.

The first one considered on August 22 was the one introduced by Senator Jacob K. Javits of New York and supported by Mr. Nixon. This Bill was defeated by a party line vote of 28 to 67, with five Republicans voting with the Democrats.

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The second Bill considered was the Kennedy-Anderson Bill providing for medical and health care for all on social security benefits regardless of income. This is the Forand-type legislation which the profession has been opposing. This one failed to pass, receiving 44 to 51, a difference of seven votes. If four democrats had changed their ballot, that bill would have passed and we would now be committed to the fundamental principle of compulsory medical care under social security.

The third bill, the Mills Bill, which the profession had accepted, then was passed by a vote of 89 to 2. This bill had modifications. It changes the social security restriction on working from $100 to $150 a month. It allows men to take a voluntary retirement at a slightly reduced rate at age 62, and it provides for health benefits to the needy aged by matching funds and aid from the federal government, *not* social security. Also the provision of putting self-employed doctors under social security was eliminated.

We do not dare relax our caution, however, because Senator Kennedy has announced he will go to the people and put the social security program across next January.

Carry On

In casting our ballots, it is imperative that we as a profession know what the outcome will be. We must select candidates who will carry out our own wishes on this question of medical care, not only for the aged but for others. The care for the aged is the popular feature now. It is the opening wedge to general medical care, *universal compulsory national health insurance.*

The Democratic platform very definitely adopts the social security system as the means through which "adequate medical care and the opportunity to achieve and enjoy good health is one of the eight rights for all Americans!" Their candidate, Senator Kennedy, was also the author of a Forand-type bill introduced in Congress.

The Republican party platform for older persons develops a contributory system for meeting medical costs, allows a choice of buying added health insurance and does not place it under social security. It proposes to liberalize social security so that older persons may still continue in productive work, and give the states more leeway in deciding how to use federal relief. Vice-President Nixon, in his acceptance speech, emphasized that medical care for the aged must not come under social security.

Both of these programs offering services and care for the elderly person have occupied great public attention in this present campaign year. This particular section of medical care could be the opening wedge to establish a complete system of socialized medicine.

The last resort of the profession now is the election in November. Each MSMS member and his people should know the implications before he casts his ballot. Each member and his family should not fail to vote.

That lost ballot could be the one to lose our birthright.

Campaign for Freedom

The officers of the Michigan State Medical Society became conscious of the tremendous implication of the political actions growing out of help for the aged, and the threat to change the whole complexion of the practice of medicine, and have established a Campaign for Freedom.

Every member of the Society was contacted personally, alerted to the threat and the conditions prevailing in Washington and elsewhere and was asked to go to work actively in preparing a counter offensive to preserve our freedom. Great numbers of letters and communications went to Washington and undoubtedly had some effect on the legislative action, even though it did not change the vote of the two Michigan Senators.

The action of the Congress has not solved this problem. Everybody has been told that efforts will be renewed in January to include the medical care of the aged—all of them—under social security, with necessary increases of costs and tax rate. The organization which we have developed for the Campaign For Freedom must continue alert. A thoroughly determined, fairly massive group of people can work miracles in the way of public opinion and public reaction.

Hypophysectomy and Retinopathy

With its increasing incidence, diabetic retinopathy has not only become a major problem in diabetic management but also is becoming the greatest single cause of blindness. The etiology of this condition is not known.

Since many severe diabetics live with their disease for many years without ocular complications, it seems likely that diabetes plus some unknown factor favors the development of retinopathy. Once it appears, retinopathy usually becomes progressively worse and may lead to total blindness. Yet the process has on occasion become arrested and in some few cases hemorrhages and exudates have completely disappeared.

This grim prognosis has led to a trial of a great variety of therapeutic measures. Poulsen's report, in 1953, of the disappearance of diabetic retinopathy in postpartum Simmonds Disease aroused an interest in hypophysectomy as a therapeutic measure. At a recent meeting, Pearson reported arrest of the progress of diabetic retinopathy in seven of fourteen cases. The details of these cases have not been published. Other authorities, although noting a lessening of the severity of diabetes as measured by insulin dosage, have been in essential agreement that there can be no assurance that retinopathy can be benefited by hypophysectomy.

At the present stage of our knowledge, reliance must be placed on rigid diabetic control as a prophylactic and early therapeutic measure. Retinitis proliferans has resisted all forms of treatment.

W. L. LOWRIE, M.D.

Physicians as Detectives of Diabetes

Too often treatment of diabetes is started months after symptoms have been first noted. Effective diabetic control could be enhanced by reducing the length of this untreated period. Frequently diabetes may be kept in a less severe form. The findings of postprandial glycosuria and hyperglycemia will detect such a case even before symptoms develop.

The purpose of "Diabetes Week" is to make the physicians and the general public aware of the necessity for regular urine examinations to detect such cases in an early stage. Mass urine examinations such as the classical survey made in Oxford, Massachusetts can be expected to yield almost one new case per hundred examined, or if applied to the entire country more than a million in the total population.

With new qualitative tests, a physician could with very little expense of time and money survey annually all of his patients for postprandial glycosuria. Special attention should be given to relatives of diabetics where a higher incidence of positive tests will be found. The physician alone has access to this selected group.

The detection of diabetes should be accepted by each physician as his responsibility before the insurance company, employer, or selective service makes the diagnosis, often in later stage of the disease.

WILLIAM L. LOWRIE, M.D.

Oral Hypoglycemic Agents

For decades, attempts have been made to control diabetes mellitus with an oral agent. Most have failed. However, since 1955, two of the sulfonylureas (tolbutamide and chlorpropamide) and phenethylbiguanide (DBI) have demonstrated reasonable safety and effectiveness. As a result, they have been widely, and perhaps overenthusiastically, used for the treatment of diabetes.

It is timely to review this mode of treatment.

The availability of these agents have made them popular with both patients and doctors. They afford an easy way out in the management of some diabetics. The patient can steadfastly refuse insulin and the doctor may dispose of the matter by prescribing the pills. In the writer's experience the use of these agents has been primarily on the demand of the patient.

Diet, adequate in all its constituents, remains the keystone of treatment for all diabetics. This particularly applies to those receiving the oral agents.

The pills are *not* a substitute for the diet.

The weight of the obese should be reduced. The failure of the patient to fully cooperate frequently frustrates this therapy. Too often inadequate instruction in the diet and a failure to appreciate the objective of treatment is the reason. About half of all diabetics can be controlled by diet alone.

The oral agents *are* a substitute for insulin. An ideal substitute should mimic the master in all respects. The oral agents fall short in this respect. All three require the presence of some endogenous insulin to be effective. Ablation of the pancreas renders these drugs impotent. Current hypotheses of these agents include the alteration of certain enzyme systems allowing suboptimal quantities of endogenous insulin to be effective (DBI), and the stimulation of partially functioning beta cells to release endogenous insulin (sulfonylureas). The important problem of ultimate complete exhaustion of these beta cells through chronic stimulation is still unanswered. Some have attributed secondary failures of sulfonylureas to this exhaustion.

Certain criteria have been established for the use of oral hypoglycemic agents: (1) The patient should have short duration diabetes. (2) Ideally, he should be over 50 years of age (maturity-type diabetes). (3) He should require less than 30 units of insulin daily. (4) He should be cooperative about his diet.

Since these agents do not mimic insulin, they have no place in: (1) The treatment of diabetic ketosis or coma, (2) juvenile diabetes, (3) pregnancy and diabetes, (4) the presence of complications as infection (even the common cold), surgery or neoplasm.

Therefore, the oral drugs offer an advantage to only a small number of diabetics; chiefly, the cooperative adult of normal weight with a recent onset of uncomplicated diabetes. Occasionally, one of the oral agents will simplify the daily routine of the diabetic who is blind or physically handicapped. Unfortunately, many blind diabetics are unresponsive to the oral agents.

The persistently obese individual needs extra help when dietotherapy alone has failed. The oral drugs can be helpful here. All diabetics on oral agents should be familiar with the use of insulin in the event of a complication.

The effectiveness of the oral agents (sulfonylureas) has been variously reported as high as 80 per cent. This, it seems, is contingent on the rigidity of criteria for control of diabetes. In the writer's experience, about 40 per cent of consecutive cases fulfilling the above criteria for use were successfully controlled with these agents. With success uncertain, physicians must be critical in their use of these agents.

The oral agents are *not* oral insulin. At present, there is no good substitute for insulin and proper diet in the treatment of diabetes. The mere lowering of the blood sugar or clearing the urine of glucose is not the sole goal in the treatment of diabetes. When insulin is indicated, the patient should not be allowed to dictate his choice of treatment, overruling the better judgment of the physician.

The oral hypoglycemics are interesting compounds and cannot be ignored, but their use is limited and must be highly selective. The unknown effect of prolonged usage of these agents must be recognized.

GEORGE C. THOSTESON, M.D.

"Security"

Let us consider the meaning of the word "Security."

When an impartial person hears two people in an argument, he frequently finds that the real difference or misunderstanding is the misinterpretation of the meaning of words.

Semasiology is the study of the meaning of words. Referring to the dictionary the word semantic is defined as pertaining to signification or meaning.

Again referring to the dictionary, security is defined as "the state of being secure." Secure is defined as free from care, safe, hence careless or over-confident, or as a person safe, not liable to become displaced, et cetera. Also, in safe custody as "In iron walls they deem'd me not secure"* or again, to seize and confine as a prisoner as "They formed a conspiracy to seize the ship and secure me."†

There is great difficulty in convincing people that security is not good for them by quoting the cost in tax dollars. This is so because, the person who is talking security points out that someone else is taxed, not the voter.

The use of the word security has become the popular and successful method of politicians to gain office by promising all sorts of Utopian states. The statement has been made that in Sweden, each election has been won by the person promising the most security.

Would it not be good politics and honest policy to try to educate the public as to the real meaning of "security?" That each time more security is gained, more freedom is lost?

The public has been taught that the word security has the opposite meaning of sin. It is universally popular to be against sin and for security. Is there some way in which we can change the popular conception of the word security to its true significance of evil and loss of freedom?

Many people who have been against socialization, as we in America view socialism, have been lured into the acceptance of socialization by the combination of the two words social and security. Again a misunderstanding of the true meaning of security.

We, as physicians, are particularly aware of the need for proper dosage. No one of us wants to eliminate all social security as it was originally proposed any more than we want to eliminate all aspirin. Too large doses of either can be dangerous. Let us try to teach everyone that security in the proper dosage has its place in the treatment of our social ills. Too much in the wrong place is poison and kills freedom.

CLAYTON K. STROUP, M.D.

*Shakespeare's Henry VI 1.

†Swift's Gulliver's Travels.

"In order that man may be persuaded to put forth the intense effort required to change chaos into order, he *must* feel that he has the necessary stature for the assignment, at least the potentialities. . . . It may appear absurd to philosophers, but in our age of specialization it is not only man's concept of matter which must come from science, but also man's concept of himself. . . . At the stage of specialization of our knowledge, to determine what is specifically human in man requires a veritable cracking of the concept of man. This cracking, in its turn, requires a concentrated effort of specialists; as much as was required for the atomic bomb. . . . If the concept is cracked, the release of spiritual energy will be voluminous enough to make physical nuclear energy behave. It might be powerful enough to light the lamps of peace and keep them burning."
—ANA MARIA O'NEILL.

Detroit Surgical Association

Abstracts of Papers

(THE JOURNAL will present summaries of the papers given at the Detroit Surgical Association's monthly meetings during the past year — with several summaries appearing in each of the fall issues.)

EXPERIENCE WITH ILEO-RECTAL ANASTOMOSIS IN ULCERATIVE COLITIS

JAMES BARRON, M.D., LAURENCE S. FALLIS, M.D. and EDUARDO CAMACHO, M.D.

Department of Surgery, Henry Ford Hospital

The operation of total colectomy in the surgical treatment of ulcerative colitis has received general acceptance by surgeons but many patients are loathe to accept a procedure that involves the formation of a permanent artificial anus in spite of the newer ileostomy technics and the development of dependable appliances. The reluctance is too often shared by their medical advisers and in the case of children by parents and guardians. As a result of this attitude too many patients are submitted to operation only as a last resort.

The generally unsatisfactory result of segmental resection, analileostomy, et cetera, has delayed development of techniques to preserve the sphincteric apparatus until interest was again stimulated by Abel and Aylett in 1956. Their preliminary and subsequent reports indicate the apparently good results of ileorectal anastomosis in a relatively large series of patients. This encouraging report led us to explore the possibilities of this procedure beginning in 1957.

The results of our experience with ileo-rectostomy in twenty-five patients is presented. Selection of patients, emphasizing indications and contra-indications, is discussed. Special attention is directed to the type of anastomosis employed in these cases and reference is made to experimental studies in this field.

THE INCIDENCE AND DISTRIBUTION OF ADENOMATOUS POLYPS OF THE COLON AND RECTUM BASED ON 1000 AUTOPSY EXAMINATIONS

T. C. ARMINSKI, M.D.

One thousand colons and 117 rectums undergoing autopsy were carefully examined for polyps. The location, size and gross characteristics of all polyps were tabulated, and microscopic sections were made of all grossly recognizable lesions.

Approximately 50 per cent of all specimens showed the presence of adenomatous polyps. The incidence after the seventh decade was three times as great as during the third and fourth decades. In the colon, approximately half of the polyps were on each side respectively. Including the rectum, approximately one-third of the polyps were in the rectum and one-third each on the right and left side of the colon. Based on the distribution found, about 40 per cent of the polyps would have been visible with a 25 cm. sigmoidoscope. Sixteen per cent of the colons had polyps over .5 cm. in diameter, and 7.1 per cent had polyps over 1 cm. in size. Both the total incidence of polyps and the size increased in the older age group. About half of the cases with polyps had single ones, and the other half multiple ones. The single polyps were equally distributed on each side of the colon. The multiple polyps were all situated on the right side in about 25 per cent of the colons; nineteen per cent on the left side and on both sides in 56.5 per cent.

EVALUATION OF BILLROTH I OPERATION WITH VAGOTOMY FOR TREATMENT OF DUODENAL ULCER

ROBERT REYNOLDS, M.D., and ROLAND P. REYNOLDS, M.D.

Because of the recent diversification in the surgical management of duodenal ulcer, it is possible to select the operation best suited for each patient.

If feasible, vagotomy is done in all our ulcer operations, and this may be accompanied by a fifty per cent resection or gastrojejunostomy. From 1952 through 1957, 237 operations were done for duodenal ulcer. Sixty-two of these operations were Billroth I, 50 per cent were vagotomies. The technique is discussed in detail. The ulcer is not necessarily removed and a gastroduodenostomy is done only if a safe anastomosis can be made. The results of this procedure have been very good, with only four per cent of patients reporting dissatisfaction. The combination of doing a more limited resection and vagotomy provides a more normal physiological approach to the ulcer problem. The immediate postoperative complications, such as nutritional deficiencies, dumping, and marginal ulcer, appear to be definitely decreased.

We recommend the Billroth I, 50 per cent resection and vagotomy as the operation of choice in those patients in whom it can be performed safely.

SOME UNUSUAL FORMS OF FAT NECROSIS IN SURGICAL PATIENTS

PAUL L. WOLF, M.D.
Department of Pathology, Wayne State University Affiliated Hospitals

Extra-Abdominal Subcutaneous Fat Necrosis.—Necrosis of abdominal fat occurs in both interstitial pancreatitis and hemorrhagic necrosis of the pancreas. It is generally agreed that the factor common to necrosis of abdominal fat is the release of activated enzymes into the abdominal tissues. Pancreatic lipase is the important enzyme in this respect. It is postulated that rupture of the finer ducts and acini is essential for the release of enzymes. Although ligation or obstruction of the pancreatic duct does not cause pancreatic necrosis, necrosis may occur if, in addition, the gland is stimulated to secrete actively.

Fat necrosis characteristically occurs in small patches. It may be seen in the pancreas as a concomitant of hemorrhagic necrosis. It may also occur as a result of traumatic injuries of the pancreas. Fat necrosis may be found in the omentum, mesentery, pancreatic fat and retroperitoneal fat tissue. In fat necrosis fatty acids and glycerol are liberated, and while glycerol is apparently absorbed, the fatty acids combine with calcium to form soaps.

Extra-abdominal fat necrosis may be due to lipase transmitted through lymphatics throughout the body. This is a rare entity. In the few cases recorded in the last few years, these lesions have been associated with acute pancreatitis, carcinoma of the pancreas and portal cirrhosis associated with pancreatitis.

A case of carcinoma of the pancreas and associated acute pancreatitis with extra-abdominal subcutaneous fat necrosis was recently observed at Detroit Memorial Hospital and is herewith reported.

Sclerema Neonatorum.—A case of nodular sclerema neonatorum which is subcutaneous fat necrosis of the newborn was recently observed at Receiving Hospital. Two types of sclerema neonatorum are nodular and generalized. The generalized form produces hard, waxlike skin. Death occurs within a week. However, the nodular form is self limited and the disease spontaneously disappears. The nodular masses are symmetrical and bilateral. Surgery should not be employed.

In nodular sclerema neonatorum, one observes deep-seated indurated areas in the subcutaneous fat. Histologic findings include degeneration, necrosis and crystallization of the subcutaneous fat together with an inflammatory reaction and fibrosis. It is possible that the disease is due to a delay in the maturation of the fat producing low oleic acid content which disposes to solidification.

THE COMBINED TREATMENT OF CARCINOMA OF THE CERVIX WITH FULL IRRADIATION THERAPY FOLLOWED BY RADICAL PELVIC SURGERY. Second Progress Report on a Series Now Numbering Ninety-four Cases.

ROBERT R. TURNER, M.D.
Department of Obstetrics and Gynecology, Wayne State University College of Medicine, and Department of Gynecology, Detroit Receiving Hospital.

Our study of the combined treatment for carcinoma of the cervix commenced in 1949 and is being made in an effort to evaluate its effectiveness as a treatment method and to ascertain its place, if any, in the over-all treatment of the disease.

A series of ninety-four cases of carcinoma of the cervix treated first with full irradiation therapy, followed in from four to fifty-two weeks after its completion with radical Wertheim operation, is presented.

The operative mortality in the series is zero. The over-all vaginal fistuli rate is 14 per cent. The incidence of ureterovaginal fistula is 5 per cent; of vesicovaginal fistula, 2 per cent; of rectovaginal fistula 4 per cent; and of combined vesicovaginal and rectovaginal fistulae, 4 per cent. Fistulate closed spontaneously in four women and were cured in four women by operation. Closure did not occur in the remaining six women, and four of them have died, three from recurrence of their malignancy.

Of the ninety-four patients, fourteen died; eight from recurrence of disease, and six of other diseases but with no evidence of recurrence of cancer at the time of death.

Residual carcinoma was found in the surgical specimens from twenty-six of the ninety-four women. Six of these have died, five from recurrence, giving a corrected survival rate of 80 per cent in the "residual group."

Sixty-eight women had no detectable residual cancer in their specimens. Three of these died from recurrence of their disease, thus giving a corrected survival rate of 95 per cent for the "non-residual group."

Carcinoma was found in pelvic lymph nodes in seven of the ninety-four patients, an incidence of 8 per cent. This is one third the incidence usually found in treatment by surgery alone. We conclude that adequate deep therapy eradicates pelvic nodal cancer in two thirds of the patients.

Our fistula rate of 14 per cent is still too high, but by decreasing radium dosage and modifying surgical technique, we are confident we shall be able to reduce it to a more respectable level.

It seems at this time that combined therapy may prove an adequate method in treatment of Stage I, II, and early Stage III carcinoma of the cervix, but final evaluation must wait further follow-up observations.

New Medical School Opens; Seven Others Planned

Seven new medical schools are in the planning stages, and one is ready to accept its first freshman class this September.

Accepting its first freshman class of 50 students this September is the just-completed University of Kentucky Medical Center in Lexington.

The Texas legislature has authorized a new medical school in San Antonio, though funds have not been appropriated. In California, New Mexico and the Twin City area in Minnesota, preliminary studies of medical needs have been completed. Surveys are beginning in Idaho, Arizona and on New York's Long Island.

New Personnel Begin AMA Duties

The American Medical Association has made several recent changes in personnel in its Division of Scientific Activities.

Foremost of these was the naming of John B. Youmans, M.D., as director of the division which was created in 1959 to coordinate all scientific activities of the association. He succeeds the late Edward L. Turner, M.D. Dr. Youmans was technical director of research for the U. S. Army Medical Research and Development Command, Office of the Surgeon General, in Washington.

Ralph Adams, M.D., who has already taken up his duties as assistant secretary of the A.M.A. Council on Medical Education and Hospitals, is serving in the area of graduate medicine education.

Glen R. Leymaster, M.D., has taken over duties as an associate secretary of the A.M.A. Council on Medical Education and Hospitals, with responsibilities in the field of medical school activities.

A. N. Taylor, Ph.D., formerly associate dean of the Medical School at the University of Oklahoma, at Norman, is the assistant secretary of the Council. He will serve as secretary of the A.M.A. Committee to Study the Relationships of Medicine with Allied Health Professions and Services.

Harold Watson, M.D., another recent addition to the Council on Medical Education and Hospitals, will serve as a full-time staff member to review intern and residency programs.

Ogden Johnson, Ph.D., took over his duties recently as assistant secretary of the A.M.A. Council on Foods and Nutrition. He will assist the council in its program of developing statements regarding foods and nutrition.

John Lewis, Ph.D., recently became assistant secretary of the A.M.A. Council on Drugs. He will evaluate and prepare data on various drugs for New and Non-Official Drugs, which is published annually by the council.

Joseph Jerome, Ph.D., is the new assistant to the secretary of the Council on Drugs and as acting secretary of the Committee on Cosmetics. His work deals with problems involving pharmacological products and organic chemistry.

Drug Firms Spend $197 Million On Research in '59 for New High

The prescription drug industry spent $197 million on research and development last year in the biggest privately financed assault on ill health in history.

The expenditure—16 per cent higher than in 1958—amounted to 7.8 per cent of the companies' pharmaceutical sales of more than $2.5 billion.

Austin Smith, M.D., president of the nationwide trade association of 140 ethical drug firms, hailed the expenditure as "a typically American example of the force of private enterprise at work for the betterment of humanity."

Dr. Smith said their third annual survey of research activities of the industry also disclosed, among other facts, that over $18 million of the total was spent outside of pharmaceutical house laboratories in the form of grants and contracts to medical schools, hospitals, research institutes and other institutions. He reported also that an estimated 100,200 chemicals, compounds and other substances were prepared, obtained and biologically tested by the industry in 1959 in its search for new and more specific medicinals.

Call AMA Conference on Disaster Care

A program by the Division of Health Mobilization of the U. S. Public Health Service will be featured at the County Medical Societies Conference on Disaster Medical Care, sponsored by the AMA Council on National Security, November 4-6, 1960 at the Palmer House in Chicago.

State medical society representatives, state civil defense authorities and other professional health and medical personnel will be briefed on the important programs being developed by the new PHS Division.

The nation's medical and health preparedness effort is being given new impetus as a result of the Office of Civil and Defense Mobilization delegation of authority to the Public Health Service to provide maximum assistance to community preparation in the health aspects of national defense.

More than Half of '60 Polio Victims Were Unvaccinated, Report Shows

More than half of those who contracted paralytic poliomyelitis this year had received no vaccination status reported by Surgeon General Leroy E. Burney.

Of the 310 paralytic cases this year on which the U. S. Public Health Service has received a vaccination report, 166 were unvaccinated, Dr. Burney said. The ratio probably applies to all of the 610 paralytic cases reported in the first seven months this year, he added.

About 14 per cent of all persons under 20 years of age have not received the vaccine; 45 per cent of those 20 to 40 years of age are unvaccinated as well as 89 per cent of those over 40.

Only three states have reported marked increases this year over 1959. Rhode Island reported 59 paralytic cases as of July 30, as against two last year. California listed 152 cases, as against 120 last year. South Carolina reported 29 cases, as against 11 in 1959.

Explain Details of Health Care Program Approved for Aged

The federal government is offering states liberal matching funds to provide health care for needy and near-needy persons 65 years of age and older.

The program, which Congress approved in the bob-tailed post-convention session, is supported by the American Medical Association and allied health groups.

Congressional approval of the federal-state program marked a victory for the medical profession and a defeat for Democratic Presidential Nominee John F. Kennedy, the AFL-CIO and other advocates of the Social Security approach to the problem.

After voting down the Kennedy plan and a separate proposal of the Eisenhower Administration, the Senate passed a modified version of a House-approved program. The modifications, sponsored by Sen. Robert S. Kerr (D., Okla.) and others, provided for increases in the percentage of federal matching funds and for administrative changes designed to facilitate state participation.

Start of the program was authorized for October 1, for those states where new state legislation is not required.

Administration of the program rests entirely with the states, subject to Federal approval in broad terms. It is up to each individual state whether it participates. Eligibility standards for beneficiaries and what health care services are provided are matters for the states to decide.

If a state so chooses, it can take care of all the health needs of an eligible beneficiary. The law authorized in patient hospital services; skilled nursing home services; physicians' services; outpatient or clinic services; home care services; private duty nursing services; physical therapy and related services; dental services; laboratory and x-ray services; prescribed drugs, eyeglasses, dentures and prosthetic de-

(Continued on Page 1568)

A NEW THERAPEUTIC ENTITY FOR DIARRHEA

LOMOTIL®

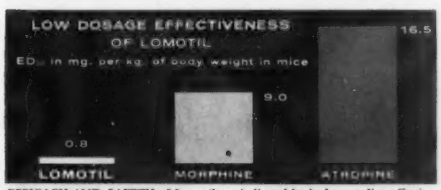
SELECTIVELY LOWERS PROPULSIVE MOTILITY

LOMOTIL represents a major advance over the opium derivatives in controlling the propulsive hypermotility occurring in diarrhea.

Precise quantitative pharmacologic studies demonstrate that Lomotil controls intestinal propulsion in approximately 1/11 the dosage of morphine and 1/20 the dosage of atropine and that therapeutic doses of Lomotil produce few or none of the diffuse untoward effects of these agents.

Clinical experience in 1,314 patients amply supports these findings. Even in such a severe test of antidiarrheal effectiveness as the colonic hyperactivity in patients with colectomy, Lomotil is effective in significantly slowing the fecal stream.

Whenever a paregoric-like action is indicated, Lomotil now offers positive antidiarrheal control . . . with safety and greater convenience. In addition, as a nonrefillable prescription product, Lomotil offers the physician full control of his patients' medication.



EFFICACY AND SAFETY of Lomotil are indicated by its low median effective dose. As measured by inhibition of charcoal propulsion in mice, Lomotil was effective in about 1/11 the dosage of morphine hydrochloride and in about 1/20 the dosage of atropine sulfate.

PRECAUTION: While it is necessary to classify Lomotil as a narcotic, no instance of addiction has been encountered in patients taking therapeutic doses. The abuse liability of Lomotil is comparable with that of codeine. Patients have taken therapeutic doses of Lomotil daily for as long as 300 days without showing withdrawal symptoms, even when challenged with nalorphine.

Recommended dosages should not be exceeded.

DOSAGE: The recommended initial dosage for adults is two tablets (5 mg.) three or four times daily, reduced to meet the requirements of each patient as soon as the diarrhea is controlled. Maintenance dosage may be as low as two tablets daily. Lomotil, brand of diphenoxylate hydrochloride with atropine sulfate, is supplied as unscored, uncoated white tablets of 2.5 mg., each containing 0.025 mg. (1/2400 gr.) of atropine sulfate to discourage deliberate overdosage.

Subject to Federal Narcotic Law.

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Research in the Service of Medicine

(Continued from Page 1566)

vices; diagnostic screening and preventive services, and any other medical care or remedial care recognized under state law.

For medical expenses of persons on old age assistance rolls, the federal government will contribute 50 to 80 per cent—with states with low per capita income getting the larger percentages of federal aid—of an amount equal to $12 multiplied by the number of old age assistance recipients in a particular state.

The matching formula will be the same for financing the health care of the near-needy but there is no $12 limitation figure.

Health, Education and Welfare officials estimated first-year costs of the program at $262 million—$202 million federal and $60 million state. Annual costs are estimated to rise by the end of the fifth year to $340 million federal and $180 million state. However, these estimates admittedly are no more than educated guesstimates because so much depends upon state action.

It was estimated that maximum participation and Michigan state contribution of $1.8 million would bring $6.2 million in federal matching funds in the first year of the program.

The medical-care-for-the-aged legislation was included in an omnibus measure titled Social Security Amendments of 1960. It also eliminated the age 50 requirement for eligibility for disability insurance benefits.

The Senate knocked out of the House bill a provision that would have brought physicians under Social Security coverage.

On other legislation of interest to the medical profession:

Congress passed bills authorizing expenditure of $10 million of counter-part funds abroad to stimulate international research; authorizing up to 15 per cent of National Institutes of Health research grants for non-governmental medical research; directing a broad study of air pollution problems; requiring informative labeling on packages of hazardous substances for household use, and giving the government power to establish a tolerance on the amount of color additives that may be used in various products.

The Senate failed to act upon House-approved legislation that would have given physicians and other self-employed persons a tax break on income put into private pension plans.

Survey Shows Ulcers More Common

More than 2.4 million Americans have ulcers, and nearly three times as many men have ulcers as do women, the Health Insurance Institute reports. Some 1,771,000 men have some form of peptic ulcer, including gastric, duodenal, and gastrojejunal ulcers, compared to 669,000 women, the Institute said.

Based on data from the U. S. National Health Survey, the Institute found that ulcers are four times as common among Americans now as they were in the 1930's.

A National Health Survey in 1935-36 showed that less than three out of every 1,000 persons in the population had an ulcer. The latest survey, covering the 1957-59 period, disclosed that 14 out of every 1,000 persons in the civilian population were so afflicted. However, this seeming quadrupling of the ulcer rate has been attributed in part to more accurate methods of diagnosis through wider use of x-ray equipment.

Other statistics, said the Institute, strengthen the impression that the prevalence rate of ulcers has quadrupled. Over a 20-year span, the rate of hospital admissions for ulcers has grown from 0.4 admissions per 1,000 persons per year to 1.7 admissions.

Three out of ten of these admissions had their ulcers treated surgically, according to the Institute.

Wanted: Books and Journals

How many times have you looked over your accumulation of not new medical or accumulated medical journals, and wished to clean the shelves? New editions have been secured, magazines have accumulated and become outdated, but your library shelves are becoming too crowded.

At long last, the project to supply much needed books and periodicals to underdeveloped libraries and medical organizations has been "test" run. The enthusiastic interest and medical associations in North Pacific and Asian countries exhibited in receiving medical books and periodicals and their willingness to place these in the libraries of their medical schools, hospitals and associations, under a "need-potential use" priority system and the co-operation of the Asia Foundation and Friends of Viet Nam in providing shipping costs, made it possible to transmit books and periodicals on a pilot-test basis early this year.

Adopt a preventive approach to the inevitable ultimatum. Prepare, or have your help-mate prepare a list of the books and periodicals you wish to share and mail this list to World Medical Association, 10 Columbus Circle, New York 19.

Shelters in Sweden

New apartment houses in Sweden provide underground protection for the occupants. The laws of Sweden require it. Often developers co-operate to blast out rock and equip one large centrally-located subterranean shelter for several apartment buildings. In one town, school, civil defense and other government authorities co-operate in planning and building a large shelter for most of the town's inhabitants.

Many Doctors Placed By Health Council

Many communities are enjoying the services of doctors of medicine this fall through the activities of the Michigan Health Council M.D. Placement Service.

There has been a general trend over the years to make the most of the placements during July and August when M.D.s finish their internships or postgraduate training programs.

The following placements were made by the Michigan Health Council during the busy summer months: C. A. Johnson, M.D., in New Era; Merle Bennett Haney, M.D., Almont; Lester Medford, M.D., Wakefield; William H. Schock, M.D., Saugatuck-Douglas; Gordon Willoughby, M.D., Alma (Locum Tenens); Charles E. Morrill, M.D., Grant; Kenneth A. Kleyn, M.D., Cheboygan; Clarence J. Kluck, M.D., Detroit; Tomas Carbonell, M.D., Centreville; David A. Wild, M.D., Manistee; John G. Lundeen, M.D., Lake Odessa; Robert E. Drom, M.D., Marquette; Warren E. Bantrager, M.D., Mio; and Juozas Sidagis, M.D., Sebewaing.

Those assisted by Michigan Health Council: William G. O'Driscoll, M.D., Grand Rapids; Robert T. Hartman, M.D., Milan; John W. Hansen, M.D., Northville (State Hospital); Tad Lonergan, M.D., Saginaw; Almon L. Schut, M.D., Kalamazoo; David Hills, M.D., St. Joseph; James Alan Gray, M.D., Battle Creek; Robert B. Marshall, M.D., Saginaw; and Leonard A. Ginnebaugh, M.D., South Haven.

Schedule Trauma Symposium

The Eighth Annual Symposium on Trauma, presented by the Wayne State University and the Detroit Academy for the Surgery of Trauma, will be held Wednesday, December 7, at the Wayne County Medical Society Building.

This year's program will consist of a series of workshop discussions of clinical problems in the morning from 9:30 to 12:00. Luncheon will be served at noon, to be followed by a series of talks in the afternoon on the surgery of trauma, presented by several leading authorities from throughout the country. The afternoon program will last from 2:00 to 5:00.

Registrations may be sent to Dr. W. W. Glass, Chairman of the Program, Director of Surgery, Wayne County General Hospital, Eloise, Michigan. House officers will be admitted at no charge.

Medical Television Shows

The Michigan Health Council reports that the following topics were covered during the month of September on the weekly Sunday morning program over WJBK-TV in Detroit: Heart Disease, Physical Therapy, Nutrition, and the Michigan State Medical Society Annual Session.

Michigan Teen-Agers to Learn About Cigarettes and Cancer

Evidence linking cigarettes and lung cancer will be studied by students in Michigan high schools taking part in a long-range educational program currently being launched nationwide by the American Cancer Society.

Centered around a filmstrip entitled, "To Smoke or Not to Smoke," and a battery of related materials for classroom use, the program is part of a broader effort to stop the skyrocketing increase in lung cancer deaths. To encourage science, biology and health education teachers to make the program a regular part of the curriculum, the Southeastern Michigan Division of the Society is offering each of the 500 schools in that area its own free set of materials, including a second filmstrip presenting the basic story of cancer as a disease and a major health problem.

Plans for initiating the program in Wayne, Oakland and Macomb counties this Fall were announced today by the Society's Southeastern Michigan Division.

Harry M. Nelson, M.D., president of the Society's Southeastern Michigan Division points out, "Present rates suggest that 1,000,000 American children now in our schools will die before age 70 of lung cancer, a disease that is fatal 19 out of 20 times. The poor prospects for detection and cure of lung cancer underscore the need to reduce our exposure to factors known to cause the disease."

The American Cancer Society and many of the nation's leading scientists accept the evidence pointing to cigarettes as an important causative factor in the 950% increase in the death rate for lung cancer since 1930. At least 23 studies in eight countries have shown that lung cancer patients are predominantly cigarette smokers.

Schedule Two CD Courses

Two national courses to train medical and health personnel for emergency services will be held at Battle Creek during the current fiscal year by the U. S. Public Health Service and the Office of Civil and Defense Mobilization.

All courses cover basic civil defense concepts, current information on biological, chemical, and radiological warfare, and community disaster planning.

Tuition and housing are provided without cost to students and approximately one-half the necessary travel expenses can be reimbursed through OCDM student training expense funds. Enrollments are limited to permit proper student-faculty ratios. Applications should be made through State Civil Defense Directors.

The courses are:

Nursing Aspects of Health Mobilization, April 23-28, 1961, by the OCDM staff and Environmental Health Aspects of Health Mobilization, April 23-28, 1961. Courses 2 and 3 held concurrently to permit joint sessions in some subjects.

Michigan Cancer Co-ordinating Committee Elects Dr. Hubly

J. W. Hubly, M.D., Battle Creek, is the new chairman of the Michigan Cancer Co-ordinating Committee. He was elected September 8 in Lansing.

H. J. Vandenberg, M.D., Detroit, was chosen vice-chairman and William J. Burns, Lansing, was re-elected secretary-treasurer. Doctor Hubly had served as vice-chairman.

Ending two years of service as chairman is H. M. Nelson, M.D., Detroit.

Members of the committee, including some newly-appointed representatives, are the following: Doctor Hubly, Doctor Vandenberg, W. A. Hyland, M.D., Grand Rapids, H. M. Pollard, M.D., Ann Arbor, and E. I. Carr, M.D., Lansing, representing MSMS; Charles F. Arnold, Detroit; William Bromme, M.D., Detroit, Michigan Cancer Foundation; John A. Cowan, M.D., Lansing, Michigan Department of Health; Nelson R. Gilbert, Lansing, L. E. Holly, M.D., Muskegon, C. Allen Payne, M.D., Grand Rapids, and Peter Wege, Grand Rapids, Michigan Division of the American Cancer Society; B. E. Luck, D.D.S., Michigan State Dental Association; Doctor Nelson and Mrs. Edward S. Wellock, Southeastern Michigan Division, American Cancer Society, and Ralph Ten Have, M.D., Grand Haven, Michigan Health Officers Association.

Heads Pharmaceutical Association

Ronald V. Robertson, practicing pharmacist of Spokane, Washington, is the new president of the American Pharmaceutical Association. Mr. Robertson assumed the office in August at the Association's 107th annual convention.

In his presidential address, he noted the outstand-

(Continued on Page 1572)

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bacteria-prone
cold

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Triaminic®, 25 mg., three active components stop running noses. Relief starts in minutes, lasts for hours.

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Calurin®, calcium acetylsalicylate carbamide equivalent to aspirin 300 mg. This is the freely-soluble calcium aspirin that minimizes local irritation, chemical erosion, gastric damage. High, fast blood levels.

TAIN brings quick, symptomatic relief of the common cold (malaise, headache, muscular cramps, aches and pains) especially when susceptible organisms are likely to cause secondary infection. Usual adult dose is 2 Inlay-Tabs, q.i.d. In bottles of 50. ℞ only. Remember, to contain the bacteria-prone cold...TAIN.

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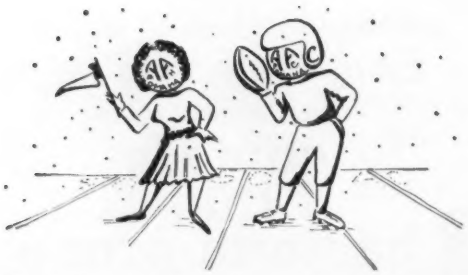

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"Notice the wonderful power of the eye in conveying ideas to the mind from writing. Take the . . . example of the numbers from one to one hundred, written down, and you can run your eye over the list, and be assured that every number is in it, and in about half the time it would require to pronounce the words with the voice; and not only so, but you can in the same short time determine whether every word is spelled correctly, by which it is evident that every separate letter, amounting to 864, has been recognized and reported to the mind within the incredibly short space of twenty seconds, or one-third of a minute."—ABRAHAM LINCOLN.

Heads Pharmaceutical Association

(Continued from Page 1570)

ing progress of community health service in recent years. He said, "It has been a breath-taking experience to witness the search for new methods of controlling disease, the dissemination of information with each laboratory triumph . . . and then to see, first-hand, the joy which has come into homes and families with miraculous swiftness.

AAMA to Meet at Dallas

Eight hundred medical assistants will attend the fourth annual national convention of the American Association of Medical Assistants in Dallas, Texas, October 14-16.

MSMS representatives to the meeting will be Glenn E. Millard, M.D., Detroit, and John W. Rice, M.D., Jackson, members of the MSMS Advisory Committee to the Michigan State Medical Assistants Society.

Two major segments of the convention program will deal with current problems and future challenges of medical practice. The morning seminar, October 15, will feature talks on "Waiting Room Atmosphere," "The Hospital, the Doctor and You" and "The Problem of Medical Care Cost in the 60's."

The "Challenge of the 60's" is the theme of the Leadership Seminar, sponsored by Lakeside Laboratories, Inc., scheduled for the afternoon. This seminar will feature lectures on credit and office management plus a round-table discussion of physician-assistant-patient relationships. Participants in the round-table will include two physicians and two medical assistants.

The AAMA, an organization whose aims and goals have been commended by the American Medical Association, has a membership of approximately 9,000 in 29 chapter states.

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1. Lippmann, O.: Arch. Ophth. **57**:339, March 1957.
2. Gordon, D.M.: Am. J. Ophth. **46**:740, November 1958.

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MICHIGAN DEPARTMENT OF HEALTH
ALBERT E. HEUSTIS M.D., State Health Commissioner

Premature Center Standards

St. Luke's Hospital at Marquette is the first facility in Michigan to receive approval as a premature center under standards recently developed by the Michigan Department of Health.

Even though many of the standards and recommendations for newborn infant care and physical facilities are set forth in the state health department *Rules and Minimum Standards for Hospitals,* special care required for premature babies prompted standards which include such considerations as specialized training of medical and nursing personnel, space allocation, environmental conditions and special equipment.

Seven per cent of Michigan's babies were born prematurely in 1959.

The standards for premature baby care call for special equipment, including incubators, where heat, moisture and oxygen may be supplied and controlled as needed. They also require careful medical supervision and nursing care of a specialized nature, including feeding techniques and protection from infection, to bring such infants through critical periods until they attain sufficient strength to survive and grow normally.

Special graduate training for medical and nursing personnel is provided by the state health department's Division of Maternal and Child Health staff in co-operation with Michigan's medical schools and schools of nursing, and through special grants from the U. S. Children's Bureau training is provided at New York Hospital, Cornell University, and the University of Colorado. In addition to the specialized training of professional personnel, the training program set up by the Child Health Section of the Division of Maternal and Child Health is offering courses for nurses aides on their role in the care of premature infants.

St. Luke's premature nursery has been given approval on a provisional basis having complied with most of the additional requirements for premature centers. Full approval will be granted as soon as additional personnel have completed the specialized courses on premature infant care.

The Michigan standards for premature infant care are among the highest in the nation.

Groups co-operating with the health department in establishing the standards included the Child Welfare Committee of the Michigan State Medical Society, members of the Michigan branch of the American Academy of Pediatrics, private pediatricians, and the Michigan Crippled Children Commission.

The Crippled Children Commission spends some $300,000 annually out of its "afflicted children funds" for the care of premature infants whose parents are not able to pay for the special care provided. Expenditures in 1959 were made for about one of every 17 of the 14,378 infants born prematurely.

In addition to the staff of St. Luke's Hospital, the Michigan State Police must be credited for the successful functioning of the premature center. Because of the widely scattered areas of population and the long distances from many areas to the premature center in the Upper Peninsula, the State Police have agreed to render assistance in transporting infants from distant points to the center at St. Luke's when other safe forms of transportation are not available.

Establishment of the premature center at St. Luke's and development of special standards for the care of prematurely born babies marks another milestone in Michigan's continuous march toward better health care for its children.

National Cancer Institute Referrals

The co-operation of physicians is requested in studies on colon and rectal carcinoma recently initiated at the Clinical Center, National Institutes of Health, Bethesda, Maryland. Encouraging results in the treatment of gastrointestinal carcinoma have been reported using the pyrimidine analogues 5-fluorouracil and 5-fluorodeoxyuridine. However, other reports have raised the question of their effectiveness.

The Chemotherapy Service of the National Cancer Institute is conducting studies of these agents in carcinoma of the colon and rectum in order to better define their place in the treatment of metastic gastrointestinal neoplasm. The side effects of these agents may be considerable so patients must be in good general condition in order to tolerate adequate doses. Also the presence of tumor masses which can be either measured directly or demonstrated on roentgen films is necessary in order to determine the antitumor effect of the drugs in short trial periods.

(Continued on Page 1584)

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In all grades of hypertension, Serpasil may be used as a background agent. By permitting lower dosage of more potent antihypertensives, Serpasil minimizes the incidence and severity of their side effects.

CIBA
SUMMIT, N. J.

*Coan, J. P., McAlpine, J. C., and Boone, J. A.: J. South Carolina M. A. 51:417 (Dec.) 1955.

Complete information available on request.

Pathology Comment

These items are provided by the Michigan Pathological Society

Cystic Fibrosis

The publication of two articles and an editorial on the subject of cystic fibrosis of the pancreas in a recent issue of the *Journal of the American Medical Association* emphasizes the new awareness with which physicians are now regarding this disease.[1] Although unrecognized until 22 years ago, it is now realized that cystic fibrosis causes more mortality among children than rheumatic fever, diabetes, or poliomyelitis.

Defect Inherited

The disease appears to be genetically transmitted as a recessive trait, and there is considerable evidence that homozygotic persons show the full disease picture and heterozygotic persons are either free from the active disease or show one or more manifestations of the disease picture. The incidence of the disease in its complete form is approximately one in 1,000 live births, equally affecting all Caucasoid groups and rare in Negroes.

The term "cystic fibrosis of the pancreas" is, of course, misleading in that the disease affects the respiratory tract, the pancreas, sweat and salivary glands. It has also been referred to as "congenital steatorrhea," "fibrocystic disease of the pancreas," and "mucoviscidosis." The latter name, first applied by Farber, refers specifically to a thick, tenaceous mucus which plugs pancreatic and salivary ducts and the bronchi.[2]

Improved Diagnostic Measure

The increase in the number of patients observed is the result of better methods of diagnosis and prolongation of the life span by effective use of antibiotics. The *markedly elevated sweat chloride*, which is a constant accompaniment of the disease process, is the most important single diagnostic feature.[3] It is of interest that about 20 per cent of relatives of known cases also have elevated sweat chloride as their only abnormal finding. In addition a significant number of relatives have frequent attacks of bronchitis or chronic respiratory involvement.[4]

Diagnostic Criteria

The screening tests for electrolytes are most meaningful when negative. Positive screening tests should always be verified by quantitative methods. Values for *sodium* in sweat above 80 mEq/L are diagnostic in about 98 per cent of cases;[5] *chlorides* above 60 mEq/L have been considered diagnostic also when accompanied by relevant clinical data.[6,7] Determination of *trypsin* may be helpful, and duodenal intubation is still valuable in the cases where there is a classic picture of cystic fibrosis with respiratory and G.I. symptoms and borderline concentrations of sweat sodium and chloride.[5] Chronic pulmonary involvement, usually confirmed by *chest x-ray*, and a *familial history* of the disease are the other major diagnostic criteria.[4]

Etiology—A New Theory

While most investigators of the disease have concentrated on the apparent malfunction of mucus-producing glands, G. B. S. Roberts has postulated that the fundamental cause is an abnormality in humoral transmission of nerve-impulses to secretory glands.[8] Normally when a gland is stimulated, acetylcholine is liberated at the nerve endings. Once liberated, its action is controlled by its break-down by choline esterase.

If the specific choline esterase were diminished in amount, or if the acetylcholine were more resistant than usual to its activity, the acetylcholine released would act for an abnormally long time and cause oversecretion of glands. Roberts postulates that cystic fibrosis is the physiological opposite of myasthenia gravis, which is due to diminished acetylcholine production or increased resistance to its activity.

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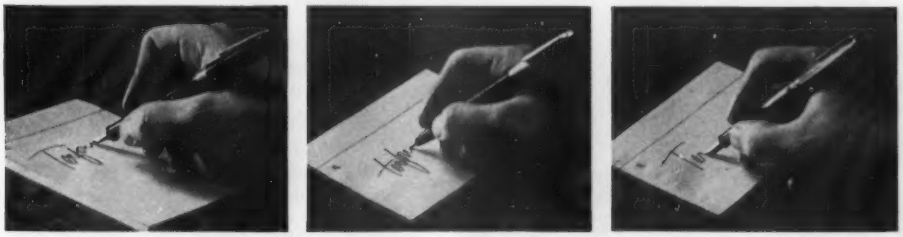

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The Michigan Diabetes Association

(Recently I had a conversation with Frank H. Jenne, Executive Director of the Michigan Diabetes Association [M.D.A.]. Mr. Jenne was asked a number of questions regarding the nature and scope of this organization. His answers were most informative and were considered appropriate for publication in this issue of the JOURNAL. *All physicians in Michigan should know about the existence of the M.D.A.*

—THE EDITOR)

Q. *What is the Michigan Diabetes Association? Isn't it fairly new?*

A. Like many other voluntary health agencies, the M.D.A. was initiated by a group of interested physicians. Although it now has two components, the Clinical Society and the Lay Society, it is organized so that the guiding direction is rendered by its physician members. In 1948 the M.D.A. was formed as a successor to the old Detroit Diabetes Association which had been active since the 1920's.

Q. *What are the roles of the component societies of the M.D.A.?*

A. The Clinical Society, which now has over 110 members, regards professional education as its primary function. To its open meetings held in conjunction with the annual assembly of the Michigan State Medical Society, the society supports a half-day postgraduate program, including outstanding speakers in the field of diabetes. The American Diabetes Association, parent organization of the M.D.A., will present its annual midwinter postgraduate course in Detroit in 1962. This year the M.D.A. will award one or two modest financial grants for the support of worthy research in the field of carbohydrate metabolism. In the future, expansion of this noteworthy effort can be expected. Along with the local medical societies, the Clinical Society is active in the annual Diabetes Detection Drive. A tremendous supporting role is played by the Lay Society during this program. Through the Lay Society, the Clinical Society directs the programs of patient and public education in diabetes. Three years ago, with no paid staff, little money and unlimited faith and energy, the Society initiated Camp Midicha, a summer camp for diabetic children. The Lay Society, with about 500 members, holds educational meetings in Detroit, and in the units now organized in Ann Arbor, Grand Rapids and Oakland County. Other similar units elsewhere in the state are being organized. The Lay Society is also active in group activities for diabetic children, discussion groups for their parents, donates volunteer service in support of the detection and camp programs, and contributes to the research fund.

Q. *Who can join the M.D.A.?*

A. Any physician or dietitian in good standing who is nominated and seconded by two present members of the Clinical Society may become a member of this society. Annual dues are only $5.00. Any non-professional person interested in diabetes and helping diabetics may become a member of the Lay Society. Their annual dues are only $2.00. The member of the Lay Society receives a regular newsletter and other informative material. Names of lay members are kept in confidence.

Q. *How do diabetics participate in diabetes detection?*

A. Every November, for one week, a drive is held to detect the undiagnosed diabetic. This detection drive is sponsored jointly by the Michigan Diabetes Association, the Michigan State Medical Society and the local county medical societies. The "Testape Dreypak" is used. This facilitates the screening (by urinalysis) of large numbers of individuals. Last year 67 new diabetics were discovered through this program.

Diabetics are asked to encourage their blood relatives to participate in this program annually. Volunteers from the Lay Society and other organizations assist in the distribution and processing of the test materials. An adequate follow-up program is essential to this detection program. All individuals with glucosuria are referred to their family physician for follow-up analysis.

Q. *Does the M.D.A. undertake diagnosis and treatment?*

A. No. All individuals who screen positive for sugar during the detection drive are referred to their family physicians for proper follow-up, diagnosis and treatment. In order to evaluate the

(Continued on Page 1582)

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(Continued from Page 1580)

program, the private physician is asked to report his final diagnosis to the M.D.A.

Q. *How is Camp Midicha for diabetic children supported?*

A. Although M.D.A. is supported in part by the Michigan United Fund, the summer camp is not subsidized. Camper's fees, memorial contributions and direct gifts support the camp. Many organizations and individuals contribute full or partial camperships for needy children. No child expressing interest is denied admission for financial reasons. The camp, located near Columbiaville, Michigan, is open for a two-week period in August. Additional support for the camp is continually sought in order to improve local facilities and lower fees for the individual camper.

Q. *What is the future of the M.D.A.?*

A. M.D.A. expects to continue its present activities on an expanded basis, reaching into all parts of the state. The frequency of diabetes in Michigan amply justifies this effort.

A Summer Camp for Diabetic Children

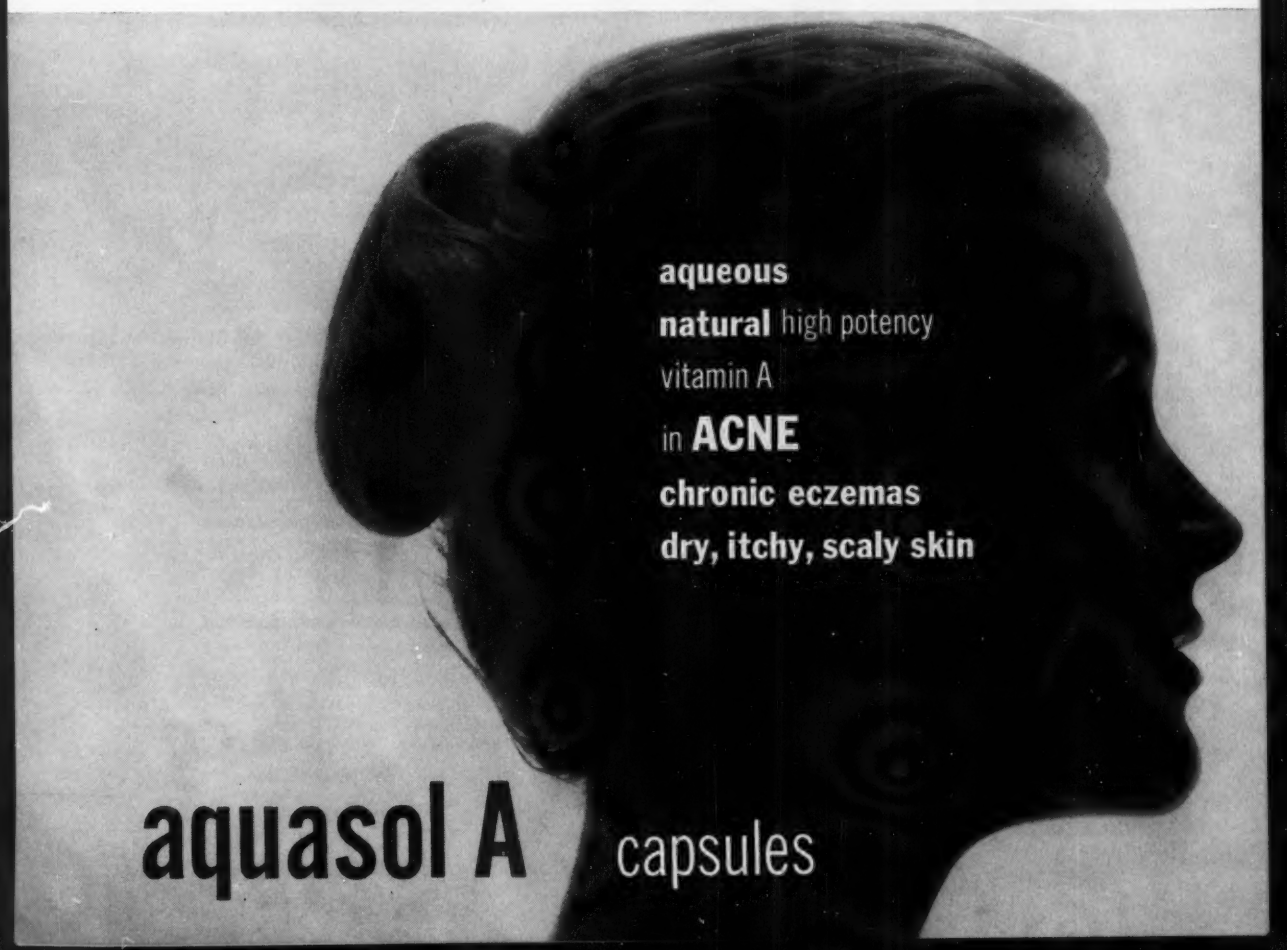
The Michigan Diabetes Association has sponsored a diabetic childrens camp for several years at Columbiaville, Michigan. It is the hope of the association that more and more physicians and parents of diabetic children will become aware of the existence and the advantages of a special camp.

This past year 70 children with diabetes attended Camp Midicha, as it is called, for the two week period.

Camp Midicha, utilizing the facilities and camping staff of Camp Tau Beta, is located a few miles north of Lapeer.

A full camping program is provided. The camp Tau Beta staff conducts the routine camping program and little alteration from their usual summer schedule for their non-diabetic campers. This is accomplished only through careful supervision by the medical staff consisting of two pediatricians, five nurses, and two dietitians.

The diet and insulin dosage are carefully balanced against each day's planned activities for the individual



child. It has been the experience of Camp Midicha that the insulin needs of at least two-thirds of the campers will vary more than ten units from the usual daily dose. However, they have never had to send a camper home because of uncontrolled diabetes.

Fig. 1. Midicha campers on kitchen police duty aid dietitian and cook.

It is the hope of the Michigan Diabetes Association that physicians and parents of diabetic children will become aware of the advantages of a diabetic childrens camp. A diabetic child often is unaware of the large numbers of similarly afflicted children. He or she feels burdened and handicapped because of the illness. However, when living in close contact with normally active diabetic children this feeling is sure to be lessened. It is to be emphasized that at Camp Midicha a normal camp life is pursued.

Another major advantage of camp life for the diabetic child is the separation from the parents. It is well known that children with chronic diseases such as diabetes become extremely dependent upon the parents and the parents become overprotective of their child. By having the child live and enjoy life away from home for a two week period, therapeutic benefit is derived for both the child and the parents.

It is the ambition of the Michigan Diabetes Association to annually enlarge Camp Midicha so that in the future a summer-long camp program may be offered to all Diabetic children of this area.

WILLIAM E. RUSH, M.D.

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Obstetrical Brevits

(This column is sponsored by the Michigan Society of Obstetrics and Gynecology.)

Puerperal Infections

In a survey of maternal deaths in Michigan made over a two and one-half year period in 1927-1930 there were 1,627 maternal deaths. Of these, 627 were attributed to puerperal sepsis, an incidence of 42.5 per cent. Infections due to abortions and following ectopic pregnancies were not included.

During the eight years, 1950 through 1957, in 624 deaths due to direct obstetric causes, there were only 88 maternal deaths due to puerperal infections, an incidence of 12.7 per cent. However, if for purposes of comparison the maternal deaths from abortion and ectopic pregnancy, of which there were 46, are deducted, there would remain only 42, an incidence of 6.7 per cent. Of these 42 deaths, 27 were due to septicemia and 15 to peritonitis.

This rather remarkable lowering of the death rate from infection can be attributed to better obstetric techniques, more frequent, prompt replacement of lost blood, the prevention of electrolyte imbalance, and the availability of antibiotic agents. Many of these deaths followed long exhausting labors, followed by traumatic deliveries, profound blood loss, and failure to maintain proper blood chemistry. In many cases the terminal sepsis might have been avoided had there been more frequent resort to consultation, better preparation of patients for cesarean section, and less reluctance to deliver abdominally, instead of permitting a prolonged labor, often terminated by a traumatic delivery and followed by severe postpartum hemorrhage.

Among the deaths from septicemia, one was a patient from whose blood stream, hemolytic, coagulase positive, antibiotic-resistant staphylococci were recovered. Another concerned a diabetic patient who appeared resistant to all forms of antibiotic therapy.

The number of infections due to organisms which do not respond to the common antimicrobal agents appears to be steadily increasing. Are we relying too much on these drugs for prophylaxis, and forgetting the time-honored, rigid aseptic techniques aimed at preventing the infection from occurring?

More careful preparation of patients for vaginal examinations, more rigid hand scrubbing, more adequate gowning and draping, and avoidance of contamination of instruments and the field of operation would make the use of prophylactic antibiotic therapy superfluous. When infection is suspected, immediate resort to bacteriologic studies by the use of smears and blood cultures should be employed. When an infectious organism is recovered, it must be subjected to bacteriologic study for identification and its sensitivity to antimicrobal materials. With this information at hand, one is capable of making an intelligent choice of a therapeutic agent for combating the infection.

TABLE I. MICHIGAN MATERNAL MORTALITY STUDY
Mortality from Puerperal Infections 1950-1957

Infected Ectopic Pregnacy	Self-induced or criminal Abortions	Peritonitis	Septicemia	Total
2	44	15	27	88

Sociologists, authorities on family living, physicians and others have for a long time considered means of combating the problem of self-induced and criminal abortions. It appears that we shall have it with us until better lay education, improved socio-economic conditions and information regarding planned parenthood are realized.

Better prenatal care, more frequent use of consultation advice, improved preparation of patients for cesarean section, avoidance of traumatic deliveries and prolonged labor, proper attention to blood chemistry, meticulous aseptic techniques, early bacteriologic studies and close postpartum supervision can still further reduce the mortality rate from puerperal infections.

National Cancer Institute Referrals

(Continued from Page 1576)

Patients can be accepted for these studies if they are ambulatory, have normal leukocyte count, renal and hepatic function and if they have metastases in the lung, peripheral lymph nodes (such as supraclavicular or cervical) or skin.

Referrals of such patients will be greatly appreciated. Physicians who wish to have their patients considered for study at the National Cancer Institute may write or call: Dr. Clyde O. Brindley or Dr. Paul P. Carbone, National Cancer Institute, Bethesda 14, Maryland. (OLiver 6-4000, Ext. 4251)

Brief and to the Point

SPEAK IN WEST—Several Michigan people spoke at the 13th annual meeting of the American Association of Blood Banks at San Francisco in August. They included Flossie Cohen, M.D., Detroit; Wolfgang W. Zuelzer, M.D., Detroit; Rosser L. Mainwaring, M.D., Dearborn; E. Eric Muirhead, M.D., Detroit; Grace F. Neitzer, Detroit; Kathryn M. Beattie, Detroit, and Emanuel Hackel, East Lansing.

* * *

SPEAKS AT MT. PLEASANT—James E. Kelly, M.D., Detroit, under the sponsorship of the Michigan Cancer Coordinating Committee, spoke at the meeting of the Gratiot-Isabella-Clare County Medical Society September 20 at Mt. Pleasant.

* * *

MEDICAL TELEVISION SHOWS—The Michigan Health Council reports that the following topics were covered during the month of August on the weekly Sunday morning program over WJBK-TV, in Detroit: Boats, Motors, and People (safe boating), The Radiologist Explains (Radiology), To Keep Them Well (child health), Sights and Sounds Around the Dental Chair (dentistry).

* * *

SENT TO CONCLAVE—As a part of a long-range plan to broaden the international battle line against cancer, four foreign doctors training as residents in Detroit hospitals attended the Fourth National Cancer Conference in Minneapolis, September 13-15 as guests of the American Cancer Society.

The Society's Southeastern Michigan Division sponsored the attendance of Parviz Sorouri, M.D., of Iran, resident in internal medicine at Henry Ford Hospital; Angelo Kambouris, M.D., of Greece, resident in general surgery at Harper Hospital; K. K. Lie, M.D., of Indonesia, resident in general surgery, Grace Hospital; and Giovanni Chiappi, M.D., of Peru, resident in general surgery, Herman Kiefer Hospital.

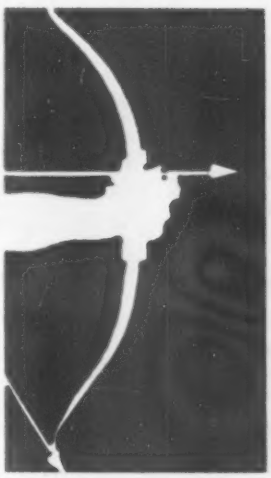
* * *

CALL CANCER MEET—The Ninth Cancer Seminar of the Arizona Division, American Cancer Society, will be held at Tucson, January 12, 13 and 14. The meeting will develop the theme of "Changing Concepts in Tumor Formation and Therapy." Chairman of the seminar is Darwin Neubauer, M.D., of Tucson.

* * *

INVITES PAPERS—The American Thoracic Society (formerly, American Trudeau Society), medical Section of the National Tuberculosis Association, is soliciting abstracts of papers on all scientific aspects of tuberculosis and nontuberculous respiratory diseases for presentation at its annual meeting in Cincinnati, Ohio, May 22-24, 1961. Abstracts must be in the hands of the program committee

Contributions for this "News Briefs" department are invited from individual physicians, from county societies, and from other health organizations. Please direct your contributions to the Editor.



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not later than January 7, 1961. For rules, write Leon H. Schmidt, Ph.D., chairman, medical sessions committee, American Thoracic Society, 1790 Broadway, New York 19, New York.

* * *

UPJOHN AIDS U-M—The Upjohn Company has provided for the University of Michigan on an extended loan basis elaborate television projecting equipment to the Medical Center. The apparatus will be used to augment present equipment for closed-circuit television of U-M medical lectures, laboratory work and clinical demonstrations. It includes an auditorium-size screen, a tele-projector and extensive servicing equipment originally purchased by the Upjohn for the medical-TV series, "Grand Rounds."

* * *

EXPLAINS ARTHRITIS QUACKERY—The danger of misleading advertised arthritis products and treatments, and what arthritis sufferers can do to protect themselves is the subject of a pamphlet available from the Arthritis and Rheumatism Foundation.

The pamphlet, "Arthritis Quackery Today," offers the facts about current misrepresentation of drugs and devices which are costing arthritics $250,000,000 each year. It includes a set of watchwords for arthritis victims and for the general public on how to recognize quackery and how to avoid it.

The pamphlet is offered by the Arthritis and Rheumatism Foundation, 10 Columbus Circle, New York 19, New York.

* * *

INTERNATIONAL NUTRITION CONFERENCE—Military and civilian nutrition experts from 19 nations attended the Fourth Armed Forces Internation Nutrition Conference held in the United States in August. Representatives of various U. S. government agencies, including the Department of Defense, Department of Agriculture, Department of State and Department of Health Education and Welfare attended. In addition, South America, Asia, Europe and Northern Africa were represented by 40 delegates attending the conference as special guests.

* * *

MEDICAL ILLUSTRATIONS—Frank H. Netter, M.D., one of the world's foremost medical artists, has signed a new ten-year contract with CIBA Pharmaceutical Products, Inc.

The new contract will assure the completion of a twenty-year Netter project of painting 20,000 color illustrations of every signification part of the body and diseases that affect it. Dr. Netter is working on the third of the nine-volume series, called "The CIBA Collection of Medical Illustrations."

* * *

SEEKS NAMES—Approximately 200 names have been given to Karl Rothschild, M.D., 747 West Seventh Street, Plainfield, New Jersey, for the list he is preparing of physicians who are descendants of veterans of the Civil War.

He seeks the names of MDs who are sons, grandsons, great-grandsons, daughters, granddaughters or great-granddaughters of veterans of the Union or Confederate Armies.

(Continued on Page 1588)

To the relief of musculoskeletal pain, new MEDAPRIN* adds restoration of function

Analgesics offer temporary relief of musculoskeletal pain, but they merely *mask* pain rather than getting at its *cause*. New Medaprin, in addition to bringing about prompt subjective improvement, promotes the *restoration of normal function* by suppressing the inflammation that *causes* the pain.

Medaprin, Upjohn's new analgesic-steroid combination, contains aspirin plus Medrol,** the corticosteroid with *the best therapeutic ratio in the steroid field*.† Instead of suffering recurrent discomfort because of the "wearing off" of analgesics, the patient on Medaprin experiences a smooth, *extended* relief and more normal mobility.

Indications: Medaprin is indicated in mild-to-moderate rheumatic and musculoskeletal conditions, including rheumatoid arthritis, deltoid bursitis, low back pain, neuralgia, synovitis, fibromyositis, osteoarthritis, low back sprain, traumatic wrist, sciatica, and "tennis elbow."

Dosage: The recommended dosage is 1 tablet q.i.d. The usual cautions and contraindications of corticotherapy should be observed.

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- 200 mg. calcium carbonate, as buffer

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(Continued from Page 1586)

The list, Dr. Rothschild explained, will not be used to establish a new organization, but may be published for informational purposes.

* * *

JUSTIN L. POWERS RETIRES—Justin L. Powers, editor of the Scientific Edition of the *Journal of the American Pharmaceutical Association* retired October 1, 1960, after many years of outstanding service. Born in Tekonsha, Michigan, on March 12, 1895, he received the Ph.C., B.S., and M.S. degrees from the University of Michigan College of Pharmacy, and the Ph.D. from the University of Wisconsin. After a long career which included faculty appointments at pharmacy schools at Washington State College, Oregon State College and the University of Michigan, Mr. Powers went to Washington, D. C., in 1940 as chairman of the APA Committee on the National Formulary. Soon afterwards he also assumed the editorship of the Scientific Edition.

* * *

NATIONAL CANCER CONFERENCE — The theme of the Fourth National Cancer Conference held September 13-15 at the University of Minnesota was "Changing Concepts Concerning Cancer." Sponsored every four years by the American Cancer Society and the National Cancer Institute, the National Cancer Conference summarized recent developments in cancer research and clinical cancer. Outstanding authorities spoke on changing concepts concerning cancer, frontiers in biology and cancer research, and care of the advanced cancer patient.

* * *

FOR GENERAL PRACTITIONERS AND INTERNISTS—Applications for Charter Membership in the American Society of Diagnostic Radiology are now being received. Membership is open to general practitioners and internists who do or may desire to do some types of Diagnostic Radiology in their offices. For further information please write Louis Shattuck Baer, M.D., F.A.C.P., 411 Primrose Road, Burlingame, Calif.

* * *

EXAM SCHEDULED—The American Board of Obstetrics and Gynecology announces that the next scheduled examination (Part 1), written, will be held in various cities of the United States, Canada, and military centers outside the Continental United States, on Friday, January 13, 1961. Reopened candidates are required to submit Case Reports for review thirty days after notification of eligibility. Scheduled Part 1 and candidates resubmitting Case Reports are required to submit Case Reports prior to August 1 each year. Details may be obtained by writing Robert L. Faulkner, M.D., Executive Secretary and Treasurer, 2105 Adelbert Road, Cleveland 6.

* * *

CONFERENCE ON NUCLEAR MEDICINE—The Society of Nuclear Medicine recently concluded its 7th Annual Meeting in Estes Park, Colorado. Approximately 500 physicians and other scientists from the United States of America and other countries were in attendance at this meeting, where over 70 papers were presented.

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Titus C. Evans, Ph.D., Iowa City, Iowa, was elevated to the presidency, and Lindon Seed, M.D., Chicago, Illinois, was chosen president-elect, William H. Beierwaltes, M.D., Ann Arbor, was elected treasurer.

The 8th Annual Meeting of the Society of Nuclear Medicine will be held at the Penn Sheraton Hotel, Pittsburgh, Pennsylvania, June 14-17, 1961.

MEDICAL MEETINGS U.S.A.

American Academy of Pediatrics, October 17-20, Palmer House, Chicago. E. H. Christopherson, M.D., 1801 Hinman Avenue, Evanston, Executive Director.

National Safety Congress, October 17-21, Chicago. R. L. Forney, 425 North Michigan Avenue, Chicago 11, Secretary.

Postgraduate course in Laryngology and Brochoesophagology, October 17-29, The Department of Otolaryngology, University of Illinois College of Medicine, Chicago, Illinois. For information write to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12.

Clinical Conference on Gynecologic Cancer, October 21 and 22, The University of Texas. M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

American Heart Association, Inc., October 21-25. Jefferson Hotel, St. Louis. Rome A. Betts, 44 East 23rd Street, New York 10, Executive Director.

Mid-West Forum on Allergy, October 22-23, Penn-Sheraton Hotel, Pittsburgh. Macy I. Levine, 3347 Forbes Avenue, Pittsburgh 13, Program Chairman.

Twenty-fifth Annual Convention of the American College of Gastroenterology, October 24-26, Bellevue-Stratford Hotel, Philadelphia.

4th Annual Postgraduate Week, October 24-28, New York Academy of Medicine, New York.

American College of Gastroenterology Annual Course in Postgraduate Gastroenterology, October 27-29, Bellevue-Stratford Hotel, Philadelphia, Pennsylvania. For further information and enrollment write to the American College of Gastroenterology, 33 West 60th Street, New York 23.

Clinical Orthopaedic Society, Inc., October, Milwaukee. Charles H. Frantz, M.D., 1810 Wealthy Avenue S.E., Grand Rapids, Secretary-Treasurer.

67th Annual Convention of Military Surgeons, October 31-November 2, Mayflower Hotel, Washington, D. C.

13th Annual Conference on Electrical Techniques in Medicine and Biology, October 31-November 1-2, Sheraton-Park Hotel, Washington, D. C.

88th Annual Meeting of the American Public Health Association, October 31-November 4, Civic Auditorium, San Francisco, California. For information write to American Public Health Association, 1790 Broadway, New York.

14th Annual Postgraduate Assembly, November 2-3, San Diego County General Hospital, San Diego, California. William Tisdale, M.D., c/o San Diego County General Hospital, San Diego 3.

Advances in Clinical Chemistry Methods, November 9-11, The Frank E. Bunts Educational Institute, 2020 East 93rd Street, Cleveland 6.

4th Annual Symposium on Diabetes, November 11, Offield Auditorium, Passavant Memorial Hospital, Chicago. The

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Chicago Diabetes Association, 620 North Michigan Avenue, Chicago 11.

American Medical Association Clinical Meeting, November 28-December 1, Washington, D. C.

American Academy of Dermatology and Syphilology, December 3-8, Palmer House, Chicago. Robert R. Kierland, M.D., First National Bank Building, Rochester, Minnesota, Secretary-Treasurer.

Conference on Handicapped Children in Michigan: Problems, Programs, and Services, February 20-21, School of Public Health, University of Michigan, Ann Arbor.

Conference on Applied Epidemiology in Communicable Disease Control, March 7-10, School of Public Health, University of Michigan, Ann Arbor.

Institute on Newer Aspects of Public Health for Health Officers, March 27-31, School of Public Health, University of Michigan, Ann Arbor.

ICE WATER RECOMMENDED AS FIRST AID FOR BURNS

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IN MEMORIAM

PAUL R. URMSTON, M.D., eighty, of Bay City, a former president of the Michigan State Medical Society, died August 24, 1960.

A native of Hamilton, Ohio, Doctor Urmston received his M.D. degree from the University of Illinois in 1903. He was an eye, ear, nose and throat specialist.

Long active in both state and county medical societies, Doctor Urmston had served as member and chairman of The Council of MSMS for several years. He was a member of the MSMS House of Delegates for fifteen years. He was a past president of the Bay County Medical Society, and was serving as medical advisor to the local group at the time of his death.

He was a member of Alpha Kappa Kappa medical fraternity.

During World War II, Doctor Urmston was in charge of Michigan's program to produce, induct and assign U. S. army medical doctors.

HERMAN BEUKER, M.D., sixty-two, Marshall physician, died August 7, 1960.

Doctor Beuker was a native of Grand Rapids and summer resident of Crystal Lake, Benzie County.

He was former chief of staff of Oaklawn Hospital in Marshall and supervised construction of the new hospital.

HENRY M. BLACKBURN, M.D., seventy, Grand Rapids physician, died August 25, 1960.

Born in Lynville, Tennessee, Doctor Blackburn had been a Grand Rapids resident forty-seven years. A graduate of Vanderbilt University School of Medicine in 1913, he received his specialized training at Rush Medical College of the University of Chicago.

He served as a captain in the Army Medical Corps, attached to the 32nd division in the Mexican border campaign and in World War I in France.

Doctor Blackburn served on the staffs of Butterworth, Blodgett Memorial and St. Mary's Hospitals.

THEODORE P. EBERHARD, M.D., fifty-six, associate radiologist at St. Joseph Mercy Hospital, Ann Arbor, since 1955, died August 14, 1960.

Doctor Eberhard was a native of Akron, Ohio. He received his bachelor's degree from the University of Akron and his M.D. degree from Western Reserve University, Cleveland, in 1930.

He did his internship in surgery in 1932 at Lakeside Hospital, Cleveland, and interned in pathology in 1933 at New England Deaconess Hospital, Boston, Massachusetts.

He was a resident pathologist with the Ponville State Cancer Hospital in Wrentham, Massachusetts, in 1934. From 1934-36, he held a fellowship in surgery at Columbia Presbyterian Hospital in New York City, where he served as an instructor in surgery in 1937. In 1939, he was an instructor in radiology at the same hospital.

From 1939-42, Doctor Eberhard was medical director of the Ellis Fischel State Cancer Hospital in Columbia, Missouri. He was on active duty with the U. S. Army Eighth General Hospital in New Caledonia from 1942-46.

In addition to Doctor Eberhard's medical society affiliations, memberships included the American Radium Society, the American Association for Cancer Research, the Arthur Purdy Scout Club, the Allen Q. Whipple Surgical Society and the Philadelphia College of Physicians. He was an honorary member of the Detroit Roentgen Ray Society and a fellow of the American College of Radiology.

JOHN W. C. FLEMING, M.D., eighty-eight, retired Pewamo physician, died August 23, 1960.

Doctor Fleming served as the village president for one term many years ago.

He was a life member and past master of Pewamo Lodge 405, F.&A.M., and a member of Scottish Rite Consistory, Grand Rapids.

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J. R. W. KIRTON, M.D., eighty-four, retired Calumet physician, died August 24, 1960.

A native of Sarnia, Ontario, Doctor Kirton came to the Copper Country in 1898. He served as physician for several mining companies in the Calumet area during the years prior to his retirement in 1947.

Doctor Kirton was a Life Member of the Michigan State Medical Society.

WARD F. SEELEY, M.D., seventy-one, obstetrician-gynecologist who had served Detroiters for forty-five years, died August 22, 1960.

Doctor Seeley received his medical degree from the University of Michigan in 1911. He came to Detroit in 1915 after four years as an instructor of obstetrics and gynecology at the University of Michigan Medical School. During World War I, he served overseas and was cited for work as a major in the Army Medical Corps.

Doctor Seeley was known as a tireless worker who stressed proper prenatal care for mothers.

In addition to other medical society affiliations, he served as treasurer of the American Association of Obstetricians and Gynecologists from 1942 until 1958.

He was a fellow of the American College of Surgeons and a past chief of obstetrics and gynecology at Harper, Herman Kiefer and Receiving Hospitals.

Doctor Seeley was a professor emeritus of medicine at Wayne State University.

He belonged to the Detroit Athletic Club and the Plum Hollow Golf Club.

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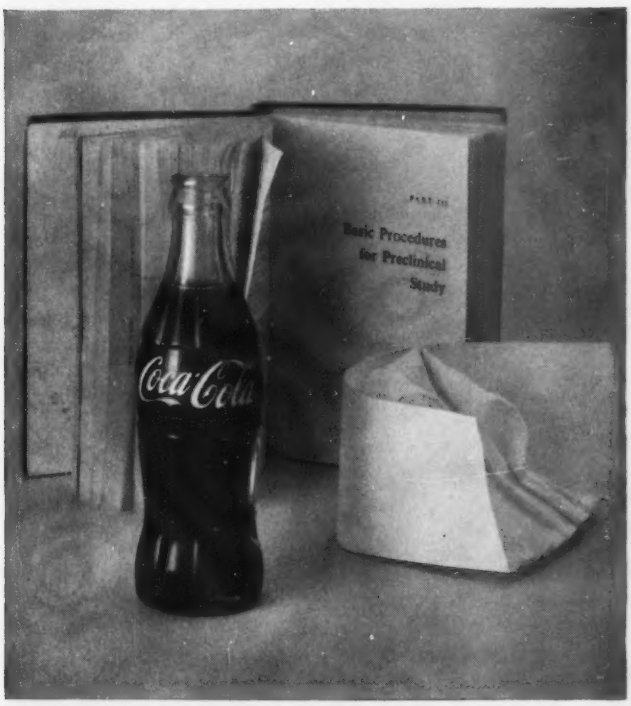

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Michigan Authors

Harry Vander Kamp, M.D., Battle Creek, "The Metabolic Error in Schizophrenia," *Medical Times*, August, 1960.

Stefan S. Fajans, M.D., John A. Moorhouse, M.D., H. Doorenbos, M.D., Lawrence H. Louis, Sc.D., and **Jerome W. Conn, M.D.,** Ann Arbor, "Metabolic Effects of Phenethylbiguanide in Normal Subjects and in Diabetic Patients," *Diabetes*, May-June, 1960.

David C. English, M.S., M.D., Jackson, "Librium, A New Non-Sedative Neuroleptic Drug: A Clinical Evaluation," *Current Therapeutic Research*, March, 1960.

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COMMUNICATIONS

Michigan State Medical Society
606 Townsend Street
Lansing, Michigan

Dear Sir:

Congratulations on the new MSMS publication, "Medical Economic Currents." It looks like an excellent job.

Sincerely,
ARTHUR KEMP, *Director*
Department of Economic Research
American Medical Association

Mr. William J. Burns
Executive Director
Michigan State Medical Society

Dear Mr. Burns:

I would like to take this opportunity to thank you, members of the medical profession, and others in Michigan who co-operated so splendidly these past two years in our effort to defeat Forand-type legislation.

It would be my personal wish to be able to write to each individual member of your organization to express my appreciation for their co-operation in winning this important battle for American medicine, but I am sure you realize this task would be most difficult in the light of many persons who assisted us.

Certainly the physicians in your State must recognize the vast amount of time and effort spent by many individual doctors in Michigan, as well as the fine work of Mr. Brenneman, Mr. Philleo and other members of your staff.

Other organizations should not be overlooked. I read many friendly editorials in Michigan newspapers and saw how well other organizations such as the Michigan Farm Bureau, Chamber of Commerce, insurance industry, etc., co-operated in this effort.

After each visit to your State, our field representative, Rueben Dalbec, reported the friendly co-operation he received from the executive office, and all with whom he visited.

Again, thanks for your help, and I hope you will kindly relay my personal gratitude to all in Michigan who helped bring about this decisive victory.

Sincerely yours,

F. J. L. BLASINGAME, M.D.
Executive Vice President
American Medical Association

September 7, 1960
Chicago, Illinois

"What unsatisfactory cases these are! This clever, charming, and widely known lady will some day disgrace us all by being juggled out of her maladies by some bold quack who by mere force of assertion will give her the will to bear, or forget, or suppress all the turbulences of her nervous system."—SIR JAMES PAGET, 1866.

Say you saw it in the Journal of the Michigan State Medical Society

EDITORIAL COMMENT

Five-Digit Figures

Bay City Times, July 3, 1960

Doting parents who dream someday of having a doctor in the family please note:

According to the Association of American Medical Colleges, medical students are currently spending some $2,911 a year for medical schooling, or $11,644 for the four-year course.

What it really amounts to, the AAMC warns, is that children of low or modest income families cannot usually aspire to the profession. And this in a day when an expanding population and growing health needs demand a continuing increase in the number of doctors.

The answer is some kind of financial assistance. What it will be—government or private—is a question that one day soon will confront the taxpayers. Not only in medical schooling but most other college education as well.

Nation Fights Novoteitis

The New Physician, October, 1960

Prominent leaders in American medicine have again warned all America against a possible epidemic of "Novoteitis," a disease affecting many adult Americans.

These same leaders point out that although vast sums have been spent on research and education since the last great outbreak in 1956, there is always a possibility of a flare-up. Because of the nature of this peculiarly American disease (of which too little is known), it can appear in many areas of the land at the same time. Although of short duration, the epidemic often leaves the nation with serious after affects.

Researchers have found, however, that immunity from novoteitis is obtained through constant vigilance. They have also determined that the disease attacks both males and females beginning at the 21-year level, although one state reported cases among 18-year-olds.

During the past four years, the study showed that "Novoteitis" is no respector of personalities, as it strikes at all levels of the nation's income groups. However, the facts show that a large number of cases occur among members of the professions, with doctors of medicine being among those often afflicted.

Temporary paralysis of the hand and loss of forward motion in the feet, both characterize the disease. Strangely enough, the diagnoses have been more readily made by political observers then by busy men of American medicine.

The implications of the above allegory are many. To the practicing profession, it is both a challenge and an indictment. To the medical student it can mean just one thing—the development and use of the strongest antibiotic known to politics—the individual doctor's vote.

Only when physicians-to-be and physicians-who-are accept their full and complete responsibilities of American citizenship, can there be hope of relief from the ravages of novoteitis—a disease welcomed by self-perpetuating politicians to the detriment of the people at large.—RFS.

Doctors Should Welcome the Test

Jackson Citizen Patriot, August 7, 1960

There is going to be much criticism of the United Automobile Workers action in setting up its own medical-care plan to compete with Blue Cross and Blue Shield. It is a step toward socialized medicine —of this there can be little doubt—and as such will be fought bitterly.

Yet we wonder if the union's "Community Health Assn." shouldn't be welcomed instead of opposed.

. . . Not because it moves TOWARD socialized medicine, but because it IS, in a sense, a preview of what socialized medicine actually will offer.

And, as such, it is going to give the American people an actual example in practice, right here, of this ogre-panacea we've been hearing so much about for so many years.

We say this not because the Citizen Patriot believes in socialized medicine but because we have faith in our medical profession as it has developed in the United States.

* * *

Before going any further, it might be well to get the ground rules for this "contest" clearly in mind. The UAW plan calls for an organized team of doctors working out of a medical group center to handle the health needs of association members.

This represents the greatest evil of socialized medicine, as its foes have been arguing for years. It means that participants will have no choice—or at the best

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a limited one—in their doctors; that day or night they will have to depend on the willingness of salaried men to serve their needs; that if they are dissatisfied with the treatment they receive, they will have virtually no recourse.

On the other hand, the UAW proposal also will provide the greatest benefits claimed by advocates of a government-run medical profession: The full facilities and abilities of trained men and splendid institutions will be made available to them; their house-call, office-call and home-nursing expenses will be paid as well as hospitalization and surgery; greater emphasis, proponents say, will be placed on preventive medicine.

The key difference between the UAW plan and government subsidy is that people are paying directly, in the form of insurance. However, this is a difference only on the surface: for, never fear, in any form of socialized medicine the people will pay.

And, once again emphasizing the "pilot project" nature of the UAW program, they will pay more under CHA (the UAW plan) then under Blue Cross, but will get more.

* * *

Thus we are going to see all the claimed evils and benefits pitted against each other in an actual operation. It's our guess that within five years the UAW program will either have faded out of the picture or have been so greatly altered as to lose most of its tinges of socialization.

Further, we would suggest to the medical profession that it spend less time making speeches against CHA and put more effort into cleaning up the abuses which have crept into its own setup and make even a pilot-run of a semi-socialized medical program possible.

"We know nothing of what will happen in the future but by the analogy of past experience. We dare not disregard the lessons of experience. We all feel that we know that a blast of wind would extinguish the flame of the candle that stands by me. How do we know it? We have never seen this flame thus extinguished. We know it because we have seen through all our lives that a blast of wind extinguishes the flame of a candle whenever it is thrown fully upon it. Again, we all feel we know that we have to die. How? We have never died yet. We know it because we know—at least we think—that of all the beings, just like ourselves, who have been coming into the world for 6,000 years, not one is now living who was here 200 years ago."—ABRAHAM LINCOLN.

Say you saw it in the Journal of the Michigan State Medical Society

The Doctor's Library

Acknowledgments of all books received will be made in this column, and this will be deemed by us as full compensation to those sending them. A selection will be made for review as expedient.

A DOCTOR IN MANY LANDS. The Autobiography of Aldo Castellani. Garden City, New York: Doubleday & Company, Inc., 1960. Price, $4.95.

This is a very interesting and entertaining book about a famous physician who practiced in many countries and associated with many notable personalities. When one wants some diversion from the scientific journals, this will be most enjoyable reading.

H.A.

MASTER YOUR TENSIONS AND ENJOY LIVING AGAIN. By George Stevenson, M.D., and Harry Milt. Englewood Cliffs, New Jersey: Prentice-Hall, Inc. 1959. Price, $4.95.

This is an excellent book for the general public explaining the cause of modern-day tensions, what to do about them and how to avoid them. The subject matter is easy reading and the many case histories holds the reader's attention.

H.A.

SIGNIFICANT TRENDS IN MEDICAL RESEARCH. Ciba Foundation Tenth Anniversary Symposium Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., Cecilia M. O'Connor, B.Sc., Maeve O'Connor, B.A. 41 illus. Boston: Little, Brown and Company, 1960. Price, $9.50.

This book is a compilation of the subjects presented concerning medical research at a symposium of the Ciba Foundation. The participants are internationally recognized authorities and the material is well selected. It would seem that the book would be of more interest to those in research and the basic sciences rather than the practicing physician.

H.A.

BIOCHEMISTRY OF HUMAN GENETICS. Ciba Foundation Symposium Jointly with The International Union of Biological Sciences. Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Cecilia M. O'Connor, B.Sc. 60 illus. Boston: Little, Brown & Company, 1960. Price, $9.50.

This is a collection of papers on the subject of Human Genetics presented at a Ciba Foundation Symposium. Since the material is up to date and highly detailed, it would be of great interest to the research workers in this field.

H.A.

THE CLONAL SELECTION THEORY OF ACQUIRED IMMUNITY. By Sir Macfarlane Burnet. Nashville: Vanderbilt University Press, 1959. Published in Great Britain by Cambridge University Press. Price, $4.00.

The Clonal Selection Theory of Acquired Immunity postulates that the unit to be considered is not the cell but the clone, that is, a group or family of cells which have multiplied asexually and so have identical genetic constitutions. This book should be of interest to those in the fields of virology, bacteriology and related subjects.

H.A.

PRINCIPLES OF PUBLIC HEALTH ADMINISTRATION. By John J. Hanlon, M.S., M.D., M.P.H., Director of Public Health Services, City of Philadelphia, and Professor and Head, Department of Preventive Medicine and Public Health, Temple University School of Medicine, Philadelphia, Pa. Third Edition, illustrated, St. Louis: The C. V. Mosby Company, 1960. Price, $10.50.

This is the third edition of this book on public health administration and new chapters on social services and addictive diseases have been added. The material is covered in a most comprehensive manner and for those interested in this subject, the book is an excellent reference work.

H.A.

NEUROSURGERY. Surgery in World War II, Medical Department, United States Army. Volume II. Prepared and published under the direction of Major General S. B. Hays, The Surgeon General, United States Army. Editor-in-Chief, Colonel John Boyd Coates, Jr., M.C. Editors for Neurosurgery, R. Glen Spurling, M.D., Barnes Woodhall, M.D. Associate Editor, Elizabeth M. McFetridge, M.A., Washington, D. C.: Office of the Surgeon General, Department of the Army. 1959. Price, $7.00.

This volume is the second in the Neurosurgical Series and deals with injuries to the spinal cord and peripheral nerves. It is a compilation by neurosurgeons who were responsible for treating these injuries during World War II and who

(Continued on Page 1600)

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(Continued from Page 1598)

have without exception established themselves as authorities in their specialty.

Part I covers injuries to the spine and the spinal cord. In this section are discussed first aid treatment, indications for laminectomy, methods of laminectomy, and post-operative care. In the post-operative care, emphasis is devoted to the urological aspects of cord injuries, decubitus ulcers, their prevention and treatment, personal and mental hygiene, and physical reconditioning.

Part II covers injuries to the peripheral nerves. In this section are discussed timing of nerve repair, methods of examining peripheral nerve injuries, anatomy, incisions, surgical approaches, and the surgical technique in most of the commonly injured peripheral nerves. Special chapters are devoted to combine bone and peripheral nerve injuries, to skin and soft tissue defects with peripheral nerve injuries, and vascular injuries with peripheral nerve injuries, and to causalgia. Physical therapy in peripheral nerve lesions and orthopedic techniques are also discussed.

The injuries discussed in this volume are seen sufficiently frequent to require complete knowledge of their care, but not so frequent in peace time to permit adequate experience. This volume gives all who handle these injuries the benefit of the knowledge and judgment of those who treated the tremendous number of these injuries in World War II. This volume is highly recommended to all who include trauma in their practice and is a must in any complete neurosurgical library.

J.C.G.

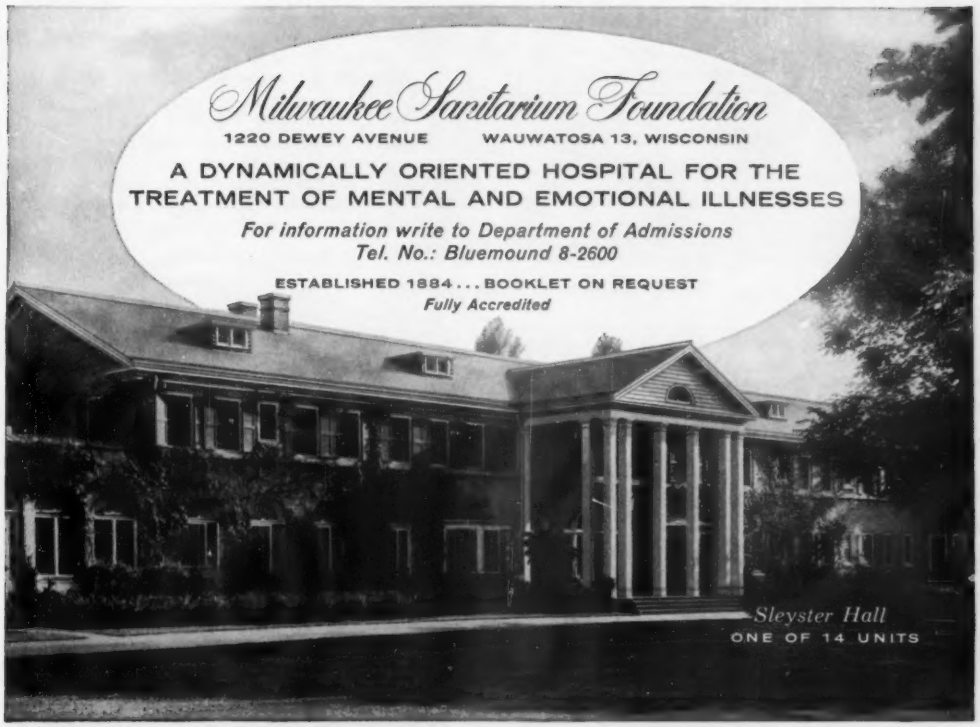
THE ETIOLOGY AND CONTROL OF PROGRESSIVE AXIAL MYOPIA. A critical, analytical, clinical study of this process from the angle of acids and proteolytic ferments and their effects upon the colloids of the eye. Also A Few Selected Papers by Hunter Heiner Turner, M.D., Nanticoke, Md. 113 pages. Privately published.

Dr. Turner, in his letter of transmittal, states he is mainly interested in protecting the vision of those unfortunates who are victims of progressive myopia. He has a most unusual explanation of the condition, gives quite a number of extensive case reports tending to support his theory that nasal and aural conditions together with salt metabolism have an influence. A challenging, interesting, and well-printed book.

NINE MONTHS' READING. A Medical Guide for Pregnant Women. By Robert E. Hall, M.D., illustrated by Robert Demarest, Garden City, New York: Doubleday & Company, Inc., 1960. Price, $2.95.

This book is primarily written for imparting general knowledge to the expectant mother and her husband. It is to be used as a supplement to the visits to her doctor. The contents encompass anatomy, physiology, hospital procedures, labor, delivery and postpartum care. Controversial issues and the newer fads are presented and fully discussed by the author. This book is very comprehensive and would be of great value to any intelligent expectant parent, both as a reference and for general information.

J.R.P.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American Medical Education Foundation 1472
Ames Co., Inc. ..... Cover III

Barry Laboratories 1586
Borden's 1508
Brighton Hospital 1595
Bristol Laboratories 1465, 1490, 1507
Burroughs Wellcome & Co. 1534-D

Central Laboratory 1593
Central Pharmacal Co. 1591
Chicago Medical Society 1572
Ciba 1577
Classified Advertising 1602
Coca-Cola 1593
Columbus Pharmacal Co. 1506

Durst, S. F., & Co., Inc. 1597

Fischer, H. G., & Co. 1600

Geigy 1504

Ingram, G. A. Co. 1486, 1590

Keeley Institute 1594

Lederle Laboratories 1495, 1534-B, 1534-C, 1581, 1590, 1594, 1598, 1602
Lilly, Eli & Co. 1512

Medical Arts Supply Co. 1588
Medical Protective Co. 1601
Merck, Sharp & Dohme 1462, 1573
Mercywood Sanitarium 1592
Milwaukee Sanitarium Foundation 1601

Noble-Blackmer, Inc. 1479

Parke, Davis & Co. ..... Cover II, 1461, 1477
Physicians Casualty & Health Association 1572
Plainwell Sanitarium 1603
Professional Management 1603

Rehabilitation Institute of Chicago 1498
Robins, A. H., Co. 1475, 1493
Roerig 1471, 1496, 1497, 1511

Sammond Pleasant Lodge 1600
Sanborn Co. 1468
Saunders, W. B., Co. 1485
Searle 1567
Smith-Dorsey 1503, 1509, 1571, 1599
Smith, Kline & French Laboratories ..... Cover IV
Squibb 1482, 1505, 1510, 1579

Tutag, S. J., & Co. 1589

Upjohn Company 1499, 1587
U. S. Vitamin & Pharmaceutical Corp. 1582, 1583

Wallace Laboratories 1466, 1467, 1500, 1501, 1534-A, 1574, 1575
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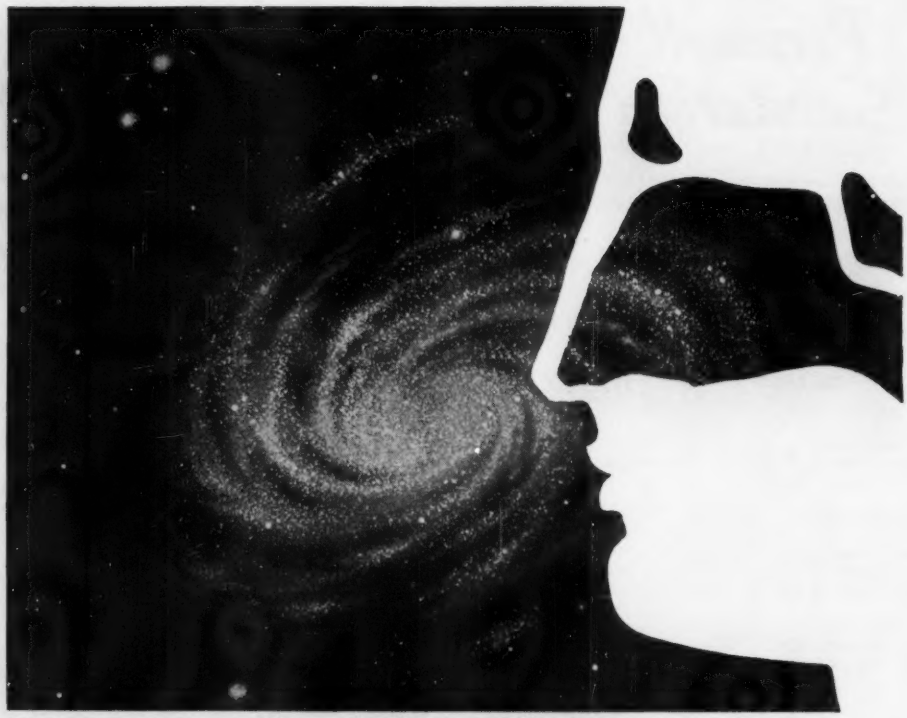

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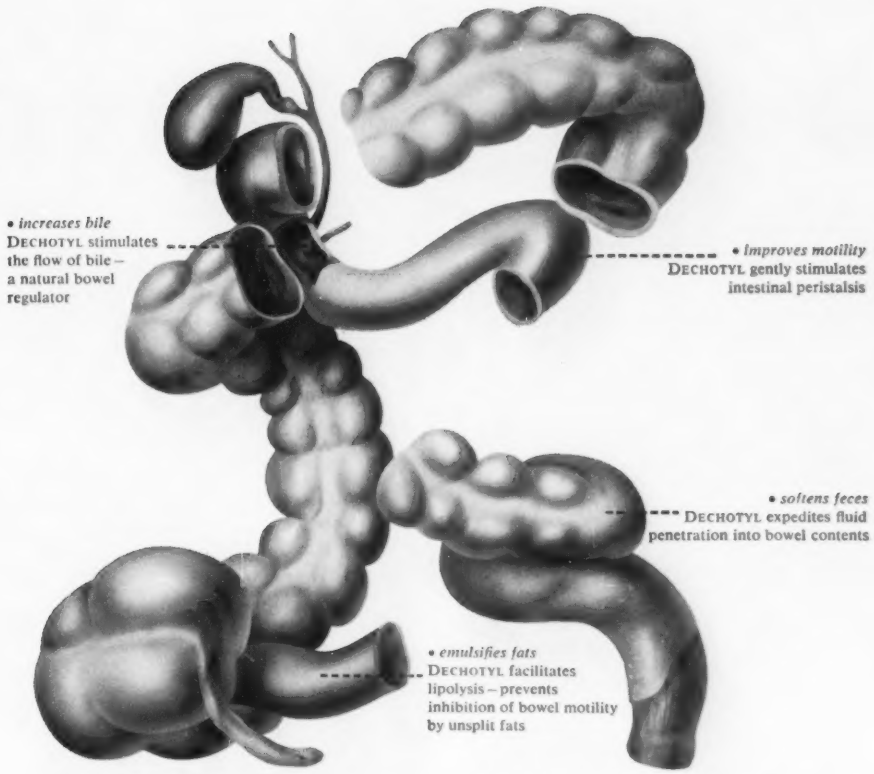
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